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VOL. 22, NO. 2 AUGUST, 1954

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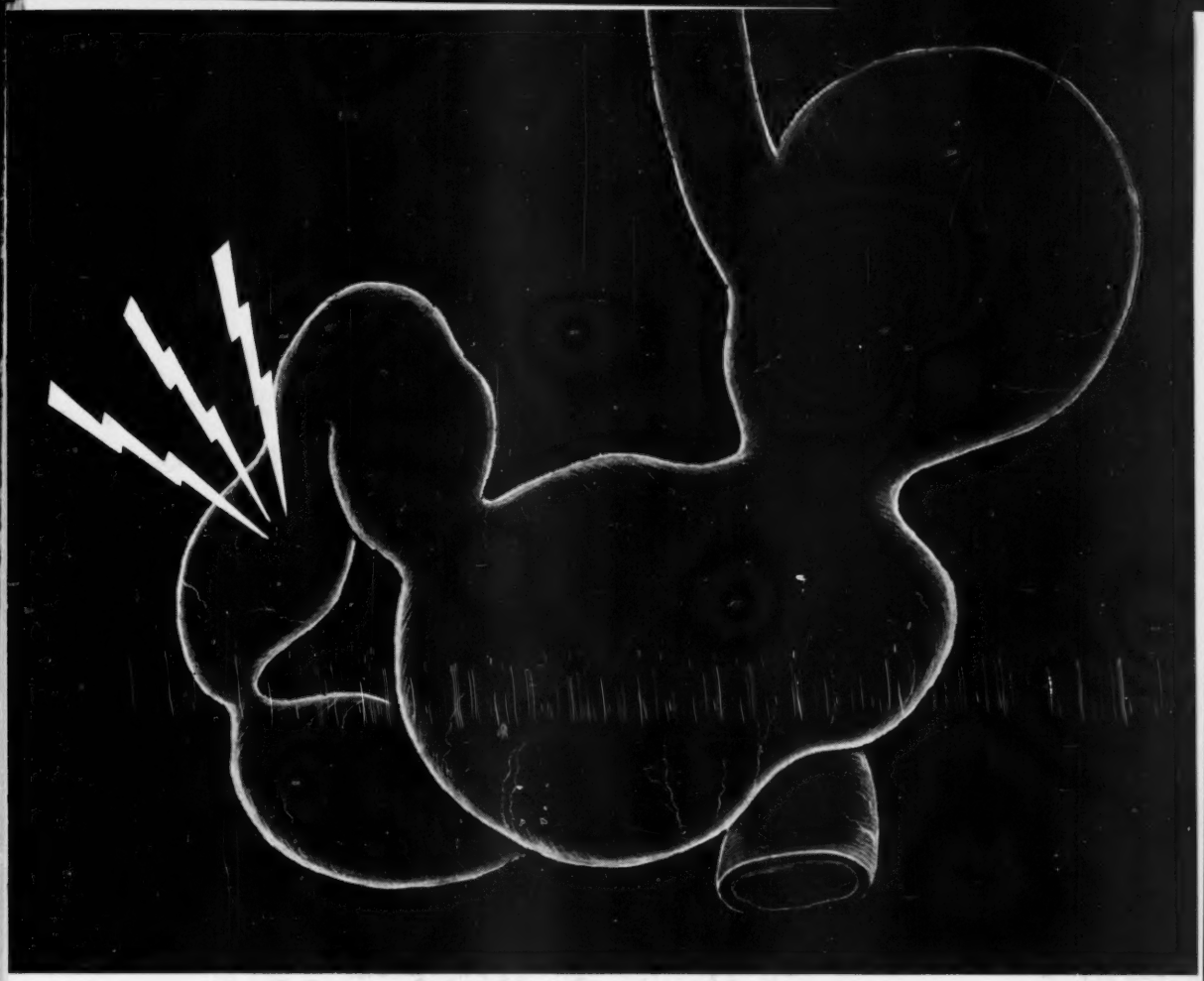

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1. Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, to be published.

2. Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., Jr., and Texter, E. C., Jr.: Mechanism of Pain in Peptic Ulcer, Gastroenterology *23*:252 (Feb.) 1953.

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The American Journal of Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

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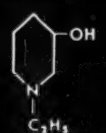

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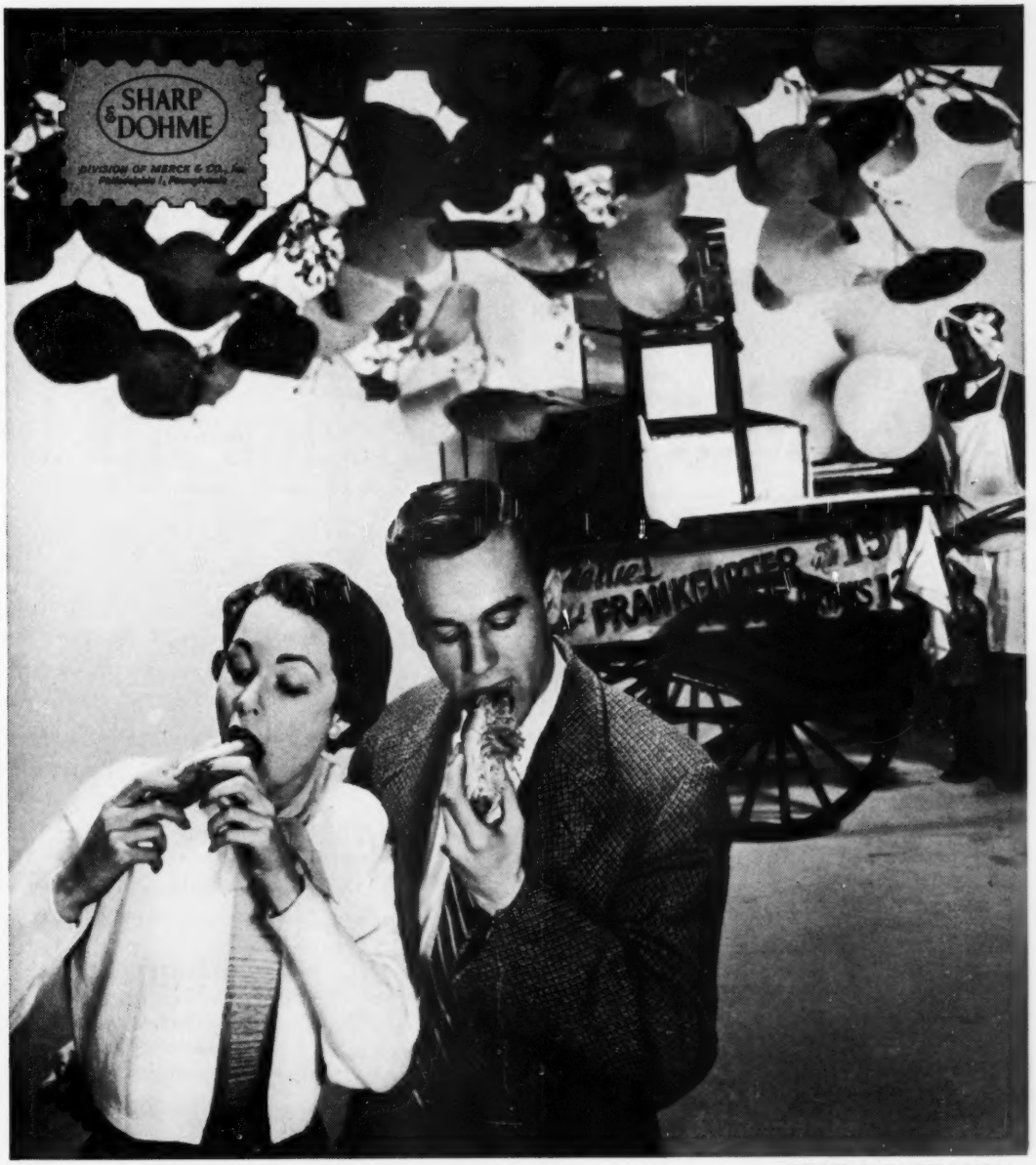

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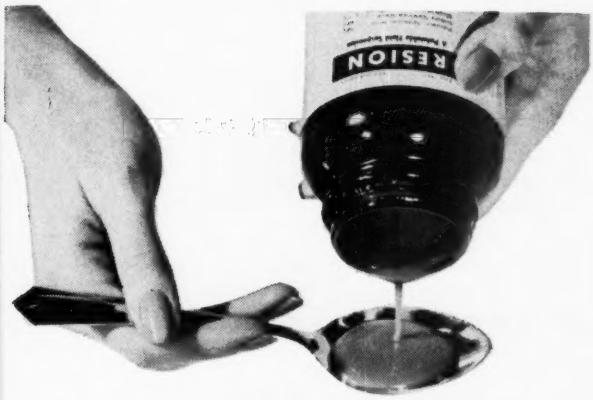

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1. O'Brien, G. F., and Schweitzer, I. L.: M. Clin. North America *37*:155 (Jan.) 1953.
2. Rising, J. D.: Missouri Med. *51*:52, 1954.
3. Lichtman, S. S.: Diseases of the Liver, Gallbladder and Bile Ducts, ed. 3, Philadelphia, Lea & Febiger, 1953, p. 49.

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VOLUME 22 AUGUST, 1954 NUMBER 2

DISEASES OF THE MOUTH*
(ORAL LESIONS)

PAUL D. FOSTER, M.D.

Los Angeles, Calif.

This paper on oral lesions is limited to those diseases peculiar to the mouth. Systemic disease manifestations will be discussed only in differential diagnosis. A thorough understanding of the conditions found in the mouth will allow the internist to better recognize systemic disease signs as they occur. A careful examination frequently gives positive clues as to the causative factors in certain local and systemic diseases such as blood dyscrasias, nutritional deficiencies, skin diseases and the occasional inflammation incident to the use of the antibiotics.

Mastication and partial digestion are the most important functions of the oral cavity. We are interested here, however, in the pathological processes of the oral cavity which contribute to generalized diseases or which are included in these systemic entities. It has been my habit to make a careful examination of the mouth in all cases of generalized eczema because it frequently gives a clue as to the causative factor. Fortunately, the mouth and its appendages are freely accessible and abnormal pathological conditions are readily visible. In examining the oral cavity, the first step is to inspect the buccal mucosa, gums, teeth, hard and soft palate, tonsils and tonsillar fossa and as much of the pharyngeal areas as can be seen by ordinary means. Growths or papular lesions should be examined manually to determine their depth and induration. Smears, serology and biopsy complete the necessary steps for the routine diagnosis.

The tissues of the oral cavity are in close relation to the external environment and by their very location and function are the receptacle of all types of contaminations. They are subject to potential irritations, infections, allergic diseases and to traumatic, chemical and thermal agents. Even though the mouth may be the dirtiest portion of the body, collectively speaking, it does show an unusual resistance to all types of involvement.

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*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, Los Angeles, Calif., 15, 16, 17 October 1953.

Embryologically, the skin and oral mucosa are derived from ectodermal tissue. It is only logical, therefore, to expect generalized skin diseases to attack the oral mucosa as well.

In the oral cavity a great number of surface lesions may be seen with similar clinical manifestations but with an entirely different etiologic and histologic picture. The diagnosis, therefore, presents many problems. Nature has been very kind in supplying us with a protective seromucous membrane and an abundant blood supply for our protection.

Before the advent of our modern laboratory technics, it was necessary to take a careful history and to observe physical findings more closely than we do at present. I have often wondered how our forefathers were able to cure any of their patients with the meagre scientific procedures they had at their disposal. We, today, with all our scientific knowledge, laboratory technics and wonder drugs rely more on these than we do our own diagnostic ability.

Periodontal disease, since it is the most frequent cause of tooth loss in the adult, deserves attention. Periodontitis is used to designate the more advanced states of periodontal disease. It refers to the inflammatory reaction of the periodontal membrane and supporting tissue, from the earliest stages of periodontal destruction to the suppurative stages in which there is marked bone loss. It is an important source of foci of infection. This source of infection may go unnoticed unless periodic x-rays are taken. The internist particularly should be constantly on guard to protect his patient from these chronic foci. The x-rays will reveal some loss of interseptal bone between the teeth as well as alveolar resorption before visible clinical evidence of periodontal disease exists. As the disease progresses, clinical signs may be seen, such as abnormal recession of the gingival tissue, packing of food between the teeth, loosening of the teeth and periodontal pockets. The periodontal pocket (pyorrhea) is produced by localized areas of destruction of the epithelial attachment and periodontal membrane. The adjoining bone and cementum is also involved. A multitude of initiating causes of periodontal diseases are well known. They include dirt, various forms of trauma, unbalanced functional occlusion, systemic disturbances, blood dyscrasias, endocrine disturbances, dietary deficiencies and infectious diseases. Normally there are no subjective symptoms such as pain, unless there is a superimposed infection present. Periodontal disease acting as a foci of infection may adversely affect the health of the patient. The presence of diabetes, nephritis, abnormal metabolic conditions or any other debilitating disease may speed up the process.

Gingivitis represents an extremely common mouth condition. The causes may be most complex and require the best of diagnostic acumen. Next to the tongue, the gingiva or gums are exposed more to outside contaminants than any other portion of the mouth. For the purposes of this paper, however, only the acute and marginal types will be discussed. The acute form of gingivitis is

associated with specific types of infections such as Vincent's Angina (fusospiroketal gingivitis) streptococcus hemolyticus, micrococcus catarrhalis or pneumococcus. Poor nutrition, alcoholism and diabetes are also contributing conditions.

Vincent's Angina (trench mouth) is the most common type of acute gingivitis and may be epidemic or endemic in occurrence. It often spreads rapidly through groups of confined people. The rapidity depends upon the virulence of the organisms and the resistance of the subjects. Most cases, however, occur singly as an acute erythematous, inflammatory condition at the gingival margin and spread rapidly to the surrounding tissues. It may involve the entire mouth including the tonsils and pharynx. Regional adenopathy is common. Depending upon the severity of the disease, the pseudomembrane which develops varies in in color from grayish-white to a grayish-green and it leaves a bleeding surface when wiped away. The constitutional symptoms depend again upon the severity and usually follow the course of any acute infection. In four to six days the periodontal tissue may become involved and there is a tendency for teeth to become loosened. There is an associated fetid odor, metallic taste and a coated, grayish tongue. The regional lymph glands may become swollen and painful. Surgical procedures about the mouth and inhalation anesthesin are, of course, contraindicated. Diagnosis depends upon the finding of the typical fusiform baccilus and spirocheta vincenti in large numbers.

Streptococci infections of the mouth, nose and throat are common and may be confused with Vincent's Angina, in the initial stages. They usually originate in the pharyngeal or tonsillar areas and spread to the gingiva. The appearance may be identical with that of Vincent's. The subjective symptoms are more severe and fever is a frequent finding. Papules, nodules or ulcerations are rare. For the diagnosis, a history of sore throat, fever and positive smears for streptococcus hemolytica or streptococcus viridans in the absence of spirocheta vincenti is sufficient.

Acute gingivitis may also result from various specific causes (localized or general) such as: 1) hot food producing a burn of the gum area, 2) chemical burns (may be the result of accidental taking of undiluted medications or using the wrong bottle or overmedication, particularly the use of iodine, silver compounds, mouth washes, or aspirin used as a local anesthetic). Further, it may be caused by improperly fitting dentures, with secondary monilia infection or by tooth brushes, tooth picks and other mechanical irritations. The appearance may be vesicular or ulcerated. The surface may be grayish white or the epithelium may be exfoliated, leaving a tender bleeding surface.

Chronic or marginal gingivitis presents no specific diagnostic microorganisms but is associated with the usual bacterial flora which is normally found about the tooth margins. The inflammation is of a chronic character and the surface epithelium is lost, leaving a reddened, swollen, soft granulation tissue covering the gingiva. It is usually very painful. There is a tendency to healing and re-

currence. This type may be caused by systemic disease and be associated with cutaneous problems that are related to allergic or endocrine deficiencies.

Dermatitis venenata or contact dermatitis such as allergic responses to nicotine; the tars from tobacco; plastic dentures and various mouth washes, tooth cleansers and medications, begins as an edematous, erythematous, painful, distressing condition of the oral mucosa. The symptoms may be minimal, involving exposed surfaces only, or severe, involving the entire mouth, throat and trachea. Unless the causative agent is found, the condition may develop into deep induration, hyperkeratosis and sloughing of the outer layers of the mucous membrane. The salivary glands become invloved, causing an elevated, papular thickening and ulceration. It is necessary to take a thorough history and to give the patients a patch-test for all known contacts. The elimination of the contact will assure rapid relief.

Painful burning tongue, in my practice, is most frequently found in middle-aged women. It is a source of great distress and should be taken seriously by the physician. It is rare to find any objective signs. The patient frequently goes to the doctor with a fear of cancer. It becomes necessary to do a complete physical and laboratory work-up to rule out the systemic diseases and endocrine problems. The first step in diagnosis being to determine whether the patient has metallic fillings and if so, the types of metal used. Dissimilar metals in an acid or alkaline media will produce a small electric current between the two metals. This electrical discharge may be measured by means of a milliammeter. Uniformity of the metals will relieve the symptoms.

Aphthous stomatitis or canker sore is a solitary or multiple, discrete (or grouped) papular lesion of the mucous membrane which produces a papule with a fibrous exudate resembling a vesicle. This area is surrounded by a hyperemic zone. the center ulcerates and early is covered with a yellowish membrane. It may occur anywhere in the mouth but is found most frequently in the folds of the mucosa. It is extremely sore and the pain is aggravated by acid foods. The biopsy findings are of little or no value and no specific organisms have ever been isolated. The initiating factors are multiple and include trauma, local infections, digestive upsets and the presence of low resistance.

A chronic type of aphthous stomatitis, called periadenitis mucosa necrotica recurrens (Sutton), is a condition that may affect any portion of the mouth. It begins with a pinhead to pea-sized, solitary or multiple, discrete, erythematous, smooth, hard and extremely painful nodule which sloughs in a few days, leaving a deep, grayish crater surrounded by intense inflammation. It is a disease which causes intense suffering. The cause is unknown. The biopsy findings are of little value and no specific organism has ever been isolated. The treatment is as varied as the number of cases diagnosed.

Mycotic stomatitis or thrush is a condition usually found in undernourished children but it may also be found in debilitated adults who have a lowered

resistance. It is associated with a deficiency of Vitamin B-complex and an achlorhydria. It is due to a yeast organism, monilia albicans. Clinically it presents whitish adherent patches suggesting a white frieze rug or curdled milk. It is not unusual for it to spread to the tonsillar fossae and pharynx and at times to the entire gastrointestinal tract. Smears and cultures are diagnostic.

Herpes simplex or herpex simplex recurrens may occur on the lips known as herpes labialis, and occasionally in the oral cavity. This lesion is initiated as groups of vesicles which rapidly break down, leaving a flat, grayish ulcer, surrounded by an erythematous area. There is a predilection for recurrence at the same site. The herpes simplex virus (which is closely associated with the smallpox virus) is the causative factor. It has been shown by Foster and Abshier that this virus and the smallpox virus are closely associated; in fact, they may be the same. Herpes simplex virus builds up a localized tissue resistance which causes the disease to remain latent for varying periods. Oral herpes is most often confused with syphilitic chancre, mucus patches, split papules, perleche, tuberculosis and diphtheria. A dark field and Wassermann will differentiate the two diseases. If the lesion is of long duration, tuberculosis must be ruled out by biopsy or cultures and smears for the tuberculosis bacillus.

Mucus patches, usually occurring on the buccal mucosa and tongue, and split papules, ordinarily at the commissures of the mouth or alveolar folds, are secondary manifestations of syphilis and are becoming relatively rare. The papillae of the mucous membranes of the tongue become edematous and swollen in discrete areas caused by the invasion of the spirochete and the resulting lymphatic white cell engorgement. The areas may appear anywhere in the mouth but most frequently are found on the tongue. The papular plaques are covered with a tenacious, slimy substance giving the appearance of small islands. The lesions are loaded with spirochetes and a positive dark field as well as a postiive serology is diagnostic of syphilis.

Perleche is an infectious, inflammatory, fissured, crusted condition of the labial commissures occurring in all ages and races. It may be confused with herpes simplex, secondary syphilitic split papules or riboflavin deficiency. It frequently gives a whitish tinge to the vermillion mucous membrane of the commissures, later becoming thickened, hypertrophic and crusted. The constant wiping of the tongue across the affected area causes irritation and extention of the process. It is caused in most cases by the monilia albicans but may be affected by a riboflavin vitamin deficiency.

Tuberculous lesions of the mouth are undifferentiated, irregular, indolent ulcers and, as a rule, do not present diagnostic features sufficient to rule out carcinoma, syphilis or other hypertrophic inflammations or ulcerous conditions. As a rule, these oral lesions are secondary to a tuberculosis of the lungs. The area involved is usually traumatized with secondary sputal contamination. A satisfactory treatment of localized tubercular lesions has been described by the author in a previous paper.

Pemphigus is a generalized systemic disease of unknown etiology but because of the high incidence of primary involvement of the oral cavity, it must be included here. It has been the experience of many dermatologists that pemphigus follows in a majority of cases some sort of dental mechanics. It appears upon the mucosa of the mouth as a clear vesiculo-bullous lesion upon a relatively normal appearing mucosa. The epithelial lining ruptures from trauma and moisture becomes secondarily infected, leaving a rough, granulomatous, erythematous, painful base. There is profuse salivation often mixed with blood and an offensive odor from the mouth. As old lesions heal, new ones develop in the mouth and the disease eventually spreads to the body, appearing as small and large bullae upon normal skin. The disease, if a true pemphigus, is fatal.

Fordyce Disease is a hereditary, congenital misplacement of sebaceous glands about the inner portions of the lips and buccal mucosa. It appears as a discrete, pinhead-sized, yellowish, maculo-papular lesion, usually loosely grouped into varying sized plaques. It is relatively common but because of the intensive cancer propaganda, patients and physicians alike are becoming acutely aware of the condition. It produces no symptoms and never, to my knowledge, becomes malignant.

Retention cysts are found on the mucous membrane of the lower lip from the alveolar fold to the vermillion border. Clinically, they appear as translucent, elevated, grayish, tense, freely movable cysts. The contents of the cysts are gelatinous in appearance and most nearly simulate "K.Y. jelly". The cyst must be destroyed either by removal or electrodesiccation, otherwise it soon recurs.

Leukoplakia is a relatively common condition of the mouth that may involve a small portion or the entire mucosa. It is characterized, in its early stages, by a faint bluish-white opaque membrane with an interlacing of fine white lines, similar to the appearance of a patch of lichen planus. Painting the cheek with a strong silver nitrate solution can reproduce a similar clinical picture. In the later stages of the disease, it presents a stark white or bluish-white, firm, often elevated, hyperkeratotic and sharply marginated membrane. No connection has been found between this and any constitutional disease. Therefore, we must assume that it is caused by local chemical, thermal or traumatic irritations. The heavy keratinization of the areas suggests that nature is attempting to protect the underlying mucous membrane. Men have a greater incidence by about 90 per cent. The symptoms vary as the condition progresses but in the order of their frequency we could classify them as: 1) cosmetic, 2) dryness or lessening of salivary secretion and 3) varying degrees of loss of taste. The text books say "look backward on syphilis and forward to cancer". The author does not feel that syphilis plays a part but does agree that leukoplakia frequently does evolve into squamous cell epithelioma. The main diagnostic problem is to rule out lichen planus, geographic tongue as well as lupus erythematosus.

Lichen planus may occur solely in the oral cavity or may be a generalized cutaneous disease. In the mouth, the eruption has a predilection for the buccal

mucosa and the tongue. The etiology is unknown but time will undoubtedly prove it to be of viral origin. I do not subscribe to the nervous tension theory and feel that nervous tension has no bearing on the disease. The lesions may be small and inconspicuous or cover large areas. They begin as pinhead to pea-sized, discrete or grouped papules usually appearing toward the anterior buccal mucosa. The primary lesion is a slightly elevated, smooth, bluish-white or gray papule. The lesion is not round but at the same time does not have the typical octagonal shape of the lichen planus papule of the skin. It can be classified as irregular in shape. The mouth lesions show Wickham's striae which are white, interlacing lines composed of ramifying striae to the adjacent mucous membrane. The areas have a tendency to coalesce and have an erythematous areola. I have never been able to observe the usual central umbilication often recorded.

Lupus erythematosus of the mouth and lips is not common but must be kept in mind in a differential diagnosis. On the vermillion border of the lips where it occurs on a transitional type of mucous membrane the diagnosis clinically is relatively easy and small spots or the entire lip may be involved. The lip becomes swollen, edematous and has a mottled bluish-gray appearance on an erythematous background. It is covered with fine, adherent scales and upon careful observation telangiectasia can be found about the margins. The mouth lesions usually are found upon the tongue and buccal mucosa. Upon the tongue, the lesions are erythematous, circumscribed and flat due to loss of filiform papillae. There is a faint whitish covering and the entire area has an erythematous halo. Similar lesions may occur upon the buccal mucosa. The etiology of lupus erythematosus is not known but for the past five years I have treated these cases with excellent results with Calciferol, Alpha Tocopherol and an acid regime.

The diagnosis of disease and the meaning of variations of the coated tongue appears to have become a lost art. The tongue, because of the filiform papillae, has a tendency to take on the color of the food eaten or medications used, as well as the color of the type of yeast organism found. A few of the more common types of coated tongue will be discussed.

Black hairy tongue has become a common condition with the more frequent use of the antibiotics. It is characterized by a swelling and elongation of the filiform papillae, anterior to the circumvalate papillae. The author has always considered this to be caused by a yeast infection. The color varies from yellow to coal black and the patients are very conscious of the condition from an esthetic standpoint even though the subjective symptoms are negligible. The type of yeast determines the color of the "hairy" patch. The use of the antibiotics causes a sterilization of the gastrointestinal tract with the exception of the yeast organisms. The yeast organisms flourish without the hinderance of the usual bacterial flora. The papillae of the tongue offers a fine, moist site for the yeast organism to grow and develop. More serious symptoms of the gastrointestinal tract may follow.

Geographic tongue (transitory benign plaques of the tongue) is a condition found in all ages and may be confused with leukoplakia, lichen planus or lupus erythematosus. It is characterized by transitory, pinhead to ½ dollar-sized, erythematous, smooth, macular plaques. The filiform papillae has been shed, leaving a flat surface and due to the fur-like appearance of the filiform papillae surrounding the area, the lesion appears depressed. The lesions extend peripherally and often present a bizarre appearance at the intersection of these peripheries. The extension of the lesions is rapid and clinical observation will make the diagnosis.

Furrowed or grooved tongue is a condition which causes patients grave concern because it frequently is associated with macroglossia and they fear the development of cancer. The disease falls into two classes, acquired and congenital. The congenital type is due to the tongue being too big for the oral cavity and of necessity it folds over upon its flat side. The acquired type, on the other hand, follows an irritation of the tongue, causing inflammation, swelling and folding. Food particles and bacteria become wedged in the furrows and this increases the irritation and produces, at times, excoriations and ulcerations. The furrows are longitudinal and forked. Many diseases have been suspect in its causation, syphilis being the most common. The author, however, feels that syphilis only plays a part when actual gumma formation can be demonstrated.

Glossitis rhombica mediana is an oval or diamond shaped, elevated, firm lesion, occurring midway between the circumvallate papillae and the tip of the tongue. It is essentially a developmental anomaly in which a portion of the base of the tongue has been interposed between the lateral halves of the tongue before fusion takes place *in utero*. Because of its prominence, firmness and elevation, it frequently becomes the source of various irritations and eventually becomes inflamed, hypertrophic and sclerosed. It is most commonly mistaken for squamous cell epithelioma.

Squamous cell carcinoma of the oral cavity constitutes 8 to 10 per cent of all cancer seen and causes 4 per cent of cancer deaths or 6,000 deaths per year, over 50 per cent being of the squamous cell type. The lower lip and tongue are the most common sites of predilection. A squamous cell cancer of the upper lip is rarely seen. The sites of cancer of the mouth are, in order: lower lip, tongue, mucous membrane of the cheek, gingiva of the mandible, soft palate, floor of the mouth, hard palate, gingiva of the maxilla. Cancer of the mucous membrane in the mouth of women is approximately 10 per cent. It occurs in the older age groups with a large majority of lesions occurring between the 65 and 70 years of age. Because of the easy accessibility to the oral cavity, early diagnosis presents a favorable prognosis. Any lesion appearing in the mouth which does not respond to local therapy should be biopsied at an early date. Due to the fact that the mucous membrane heals easily and quickly, it is well to take a fairly large piece of tissue for the biopsy, including the growth, as well as some of the normal tissue adjacent. Both lip and mouth cancer spread to the regional lymph

nodes of the neck which should always be carefully examined. In practically all cases there is an inflammatory reaction from secondary infection. The grade of the lesion is very significant, particularly in the matter of treatment. If the cells are well differentiated, chances for cure are good; if the cells show disorientation, hyperplasia and a great change in staining characteristics, then the prognosis is bad. The surgeons usually advocate removal by surgery and radiologists advocate treatment by x-ray or radium. It has been my custom to remove the lesion surgically and use radium following the surgery. If lymphatic involvement is present, a biopsy should determine the necessity for a radical resection. Squamous cell epithelioma of the tongue has a greater tendency to metastasize than lesions in other parts of the mouth.

Cancer of the tongue usually begins as a glossitis; a small, firm lesion develops which does not spontaneously disappear and which gradually becomes firm and begins to enlarge as the malignant process progresses. The tongue is composed of two sections with a median raphe, each side having its own blood and nerve supply. The lymphatics, however, have free access from one side of the tongue to the other, making contralateral metastases common.

Cheilitis, or inflammation of the vermillion surface of the lips, comes in two forms; the first, cheilitis exfoliativa is an erythematous, fissured condition of the lips, especially the lower lip. Constant exfoliation of the vermillion portion of the lips is the general rule. The patients complain of tenderness, burning and a crawling sensation. The severity varies greatly from day to day and from patient to patient.

The etiology is in doubt but many factors play important roles. The disease is most common in middle-aged women. Many writers have advocated the neurogenic theory, others claim it is the same as seborrheic dermatitis and point to the associated seborrhea of the scalp. Actinic rays undoubtedly play a part especially when the condition is limited to the lower lip.

The author feels that in those cases affecting both the upper and lower lips, mouth breathing plays the most important role. It has been his experience that all severe cases sleep on their backs and breathe through the mouth constantly, subconsciously wiping the lips with their tongues for moisture.

The second form is cheilitis glandularis (apostematosa), a congenital condition of the lips involving the labial mucous glands and ducts. Normally one or both lips are edematous and present hyperplasia of the mucous glands as widely dilated openings on the vermillion borders. There is a sticky, mucus secretion exuded from these openings which cause the lips to adhere to each other. The glands are easily palpated and frequently become infected, inflamed, suppurative and painful. Occasionally other mucus glands are involved. The treatment is unsatisfactory. Neither x-rays, electrodesiccation or excision are permanent cures.

THE PROBLEM OF ADVANCED ACID PEPTIC ESOPHAGITIS*†

J. HOWARD PAYNE, M.D.
W. RUSSELL SMITH, M.D.
and
CLARENCE J. BERNE, M.D.
Los Angeles, Calif.

INTRODUCTION

The surgical treatment of advanced acid peptic esophagitis presents difficult, complex and unsolved problems. Surgical procedures which destroy the "cardial sphincter mechanism" expose the patient to the dangers of esophagitis, ulceration, hemorrhage, perforation and stenosis unless achlorhydria exists. Likewise, medical management has not been uniformly successful in relieving the obstruction or preventing extension of the esophagitis. In this paper we intend to discuss the poor results obtained at the Los Angeles County Hospital following the operation of cardioesophagectomy for stenosis of the distal esophagus due to regurgitation of gastric juice containing acid and pepsin. In addition, we wish to stress the importance of early recognition and surgical treatment of esophageal hiatal hernia before therapeutically resistant esophagitis develops.

With few exceptions the reports in the literature indicate unsatisfactory results from operations on high grade benign stenosis of the lower esophagus. Barrett and Franklin[3] reported that of 19 patients who had esophagogastrostomy only three were clinically well. Ripley, Olsen and Kirklin[10] report that of 65 patients at the Mayo Clinic who had either esophagogastrostomy or cardioplasty, 28 had positive signs and 12 had presumptive signs of reflux esophagitis or stenosis.

Esophageal hiatal hernia is a rather common condition. Many are not detected because they are asymptomatic, overlooked, or not suspected. When the symptoms are severe, surgical correction is considered[1,12,13]. We wish to make a strong plea for surgical repair before the devastating complications occur. The symptoms of hiatal hernia; dysphagia, regurgitation, substernal pain, heart burn, and bleeding can all be reproduced by acid peptic esophagitis. Often the pain will have the time and location sequence of angina pectoris[1,4,12,13].

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†From the Department of Surgery, University of Southern California School of Medicine and the Los Angeles County Hospital.

Anatomy and Physiology

The precise functional mechanism of the cardioesophageal junction has never been clearly described. Helvetius (1719) probably was the first to mention the existence of a constrictor mechanism of the cardia. Since that time the literature has contained many conflicting opinions. Reich (1925) as quoted by Lerche[9] states, "It is difficult to get a clear conception of the closing-mechanism between the esophagus and stomach from the literature, because the numerous authors who have elaborated on this subject agree on one point only—that a closing mechanism must exist". Lerche[9], however, is convinced that the mechanism first described by Helvetius is the "constrictor cardiae". After digital examination at the time of operation, Wangensteen[14] states that in spite of no visible evidence, he feels sure that there is a functional sphincter at the esophagogastric junction.

Allison[1], however, emphasizes the action of the right crus of the diaphragm which encircles the esophagus. When contracted, it not only compresses the wall of the esophagus from each side but pulls the esophagogastric junction down and thereby increases the normal angulation of the esophagus as it enters the stomach. Ingelfinger and Kramer[7] have recently presented their interesting observations of the constriction ring in the esophagus 1 to 2 cm. above the diaphragm and suggest it might actually be the inferior esophageal sphincter.

If the intrinsic mechanism is ineffective or has been altered by unphysiological surgery the action of the diaphragm may not be enough to prevent reflux. In addition, when the extrinsic mechanism (right crus) is impaired by the dilatation secondary to hiatal hernia, another mechanism for regurgitation develops.

The consensus is that the primary function of the cardial mechanism is to allow swallowed material to pass from the esophagus into the stomach and to prevent reflux of gastric contents into the esophagus. This has been described as maintenance of "unidirectional flow". Without the combined influence of the "constrictor cardiae", diaphragmatic action, peristaltic activity, esophageal secretions and gravity, esophagitis from regurgitated gastric juice would be the rule[6].

Etiology

Ferguson, et al[6] and others[5] have published rather convincing evidence that esophagitis, ulceration, bleeding, perforation and stenosis can result from regurgitation of acid pepsin containing gastric juice into the esophagus. Hydrochloric acid in the same concentration as found in the gastric juice has much less effect on the esophagus[6]. This regurgitation occurs in patients with hiatal hernia or when the hiatus or the esophagogastric junction has been altered or destroyed incidental to surgical correction of esophageal stenosis or of achalasia.

The frequent association of duodenal ulcer, hiatal hernia and esophageal stenosis suggests hyperacidity as an important associated factor. Pepsin acts only in an acid medium. Ectopic gastric muscosa, vascular deficiency, malnutrition, infection, and neurogenic causes are other factors which are discussed as possible etiologic factors of esophagitis but are not strongly supported. Barrett and Franklin[3] have described four separate types of esophagitis. The first "inflammation due to regurgitation of gastric contents from the stomach into the lower esophagus". The second is "peptic ulceration of the esophagus occurring in an islet of ectopic gastric mucosa". The third "acute ulceration" which they state may complicate "any operation upon the esophagus in which both vagi have been divided". The fourth type "retention ulceration" which may be found in "advanced cases of cardiospasm before operation".

Material

Several surgical procedures have been tried for the correction of advanced acid peptic esophageal stenosis. The most common has been resection of the strictured area with an incidental vagotomy. Re-establishment of the gastrointestinal continuity requires an intrathoracic anastomosis between the remaining esophagus and stomach. This creates an unphysiological situation. The acid peptic gastric juice has free access to the unprotected distal esophagus and the process of inflammation, ulceration, occasionally perforation and stenosis are all recreated. Testifying to the truth of this are the poor results reported in the literature. In an effort to evaluate our results at the Los Angeles County Hospital this study was undertaken. During the five-year period of 1948 through 1952, twelve patients with acid-peptic esophageal stenosis were treated by operation at the Los Angeles County Hospital. Eight of these had an associated esophageal hiatal hernia (Table I). The remaining four (Table II) had only esophagitis and stenosis in common.

Results

Seven of the patients (Table I) had a resection of the strictured area with an anastomosis between the remaining esophagus and the cardiac end of the stomach. In this group there were three surgical deaths. Two of the deaths occurred on the fourth postoperative day. One of the two had atelectasis, pneumonitis and three centimeters distal to the anastomosis there was a two centimeter area of necrosis and perforation of the posterior wall of the stomach. The cause of this is not known for certain but many represent the place where a "Babcock" clamp had been used to hold the stomach. The other patient that died had a perforation at the suture line due to a necrotizing ulceration in the posterior aspect of the esophagogastric anastomosis. This patient had extremely high gastric acids. The third death occurred after 4 weeks, following a secondary procedure consisting of an enteroanastomosis for observation of the initial complementary gastrojejunostomy. Of the remaining four cases, two died at the end

of two years of malnutrition due to recurrent stenosis. Of the remaining two patients with cardioesophagectomies, one has been asymptomatic for one year and the other was asymptomatic for 9 months when he died of heart disease.

The patient with a hiatal hernia and an incomplete stenosis was treated with a longitudinal incision and transverse closure type of cardioplasty. The hernia was not repaired. After three years the patient remains asymptomatic.

TABLE I

Case	Disease	Operation	Results				
			Asymptomatic	Esophagitis	Stenosis	Bleeding	Death
1	Stenosis Hiatal Hernia	Cardio-esophagectomy	No	Yes	Yes	No	2 Years
2	Stenosis Hiatal Hernia	Cardio-esophagectomy	No	No	No	No	4th P.O. Day Respiratory
3	Stenosis Hiatal Hernia	Cardio-plasty	3 Years	No	No	No	
4	Stenosis Hiatal Hernia Duodenal ulcer	Cardio-esophagectomy Gastro-enterostomy	No	Yes	Yes	Yes	1 Month Malnutrition
5	Stenosis Hiatal Hernia	Cardio-esophagectomy	No	Yes	No	No	4th P.O. Day Anastomosis Perforated
6	Stenosis Hiatal Hernia	Cardio-esophagectomy	1 Year	No	No	Yes	
7	Stenosis Hiatal Hernia	Cardio-esophagectomy Pyloro-myotomy	9 Months	No	No	No	
8	Stenosis Hiatal Hernia	Hernioplasty, vagotomy, gastro-enterostomy, cardio-esophagectomy	No	Yes	Yes	No	2 Years Malnutrition

Case 8 had a hiatal hernia and an incomplete esophageal obstruction which was treated by hernioplasty, vagotomy, and a gastric drainage procedure. After a temporary period of relief the hernia recurred and the stenosis progressed. A cardioesophagectomy was done in an effort to improve the situation. There was progressive esophagitis, stenosis, deterioration, and finally death from malnutrition after two years.

The first of the four cases without demonstrable hiatal hernia (Table II) had a perforated duodenal ulcer closed in 1934. There was progressive dysphagia following this and six months later a gastrostomy was done. Fourteen years later the patient entered the Los Angeles County Hospital with a gastrostomy and a complete obstruction of the distal esophagus. A cardioesophagectomy and vagotomy was done. There was no complimentary drainage procedure. The patient was symptomatic and at the end of one year had an 85 per cent four-hour gastric retention. This gradually improved and after two years the patient was asymptomatic.

The second case had achalasia with a sigmoid type of esophagus, stasis esophagitis and partial esophageal obstruction. A cardioplasty (Wendel, Heineke-

TABLE II

Case	Disease	Operation	Results				
			Asymptomatic	Esophagitis	Stenosis	Bleeding	Death
1	Stenosis Duodenal ulcer Gastrostomy	Cardio-esophagectomy	Last 2 years	First year	No	No	
2	Stenosis Achalasia Esophagitis	Cardio-plasty ¾ Proximal Gastrectomy (10 months later)	No	Yes	Yes	Yes	
3	Stenosis Esophagitis Cardio-esophagectomy	Resection of Post-surgical stricure	Yes	No	No	No	
4	Stenosis Esophagitis	Esophagogastrostomy Side-to-side	No	Yes	Yes	Yes	2 Years Malnutrition

Mikulicz) was done followed by esophagitis and ulceration. Ten months later he was subjected to an extensive proximal gastrectomy with an esophago-antral anastomosis. A pyloroplasty was not done because the surgeon did not consider it necessary. The esophagitis continued and after one year there was severe ulceration with bleeding requiring several blood transfusions. On a strict medical regimen his general condition is now stationary but esophagitis is still present.

The third case had esophagitis with stenosis for five years. A cardioesophagectomy was done at an outside hospital. There was progressive obstruction at the anastomotic site and five months later the strictured area was excised and another esophagogastric anastomosis was accomplished. This patient has mild epigastric complaints.

The last case developed increasing dysphagia and intermittent vomiting in the seventh month of pregnancy. This continued for eight years at which time a side-to-side esophagogastrostomy was done, sidetracking the stenosis. The esophagitis continued and after two years the patient entered the Los Angeles County Hospital but expired in 24 hours from massive esophageal hemorrhage. At autopsy a 12 cm. ulceration was present in the distal esophagus.

Comment

It is apparent that our experience with present day methods indicates that they are frequently inadequate to control the problems presented by advanced acid peptic esophageal stenosis. From the data presented two factors are conspicuous. First, surgical correction of a lower esophageal stenosis is associated with a high mortality and morbidity. Second, any procedure which destroys the sphincter mechanism very strongly predisposes to recurrent esophagitis, ulceration, perforation, bleeding and stenosis unless a high grade hypochlorhydria exists. Any form of surgery for control of esophagitis must keep the gastric juice out of the esophagus[6]. With this in mind, it is apparent the surgical approach must be altered in two general aspects. First, because early acid peptic esophagitis secondary to hiatal hernia is usually eliminated by surgical correction of the hernia, this procedure should be instituted as soon as such a situation is recognized. Such a patient should never be allowed to progress to the point of high grade esophageal obstruction. Second, we must recognize early the patient with a duodenal ulcer complaining of dysphagia or any of the other symptoms or signs of acid peptic esophagitis. The therapeutic approach in this instance is to reduce the acid-peptic factor. In the past we have relied upon three procedures; a proximal three-fourths subtotal gastrectomy with esophagoantral anastomosis, a distal subtotal (three-fourths) gastrectomy or a vagotomy with pyloroplasty. In the latter two procedures, repair of the coexistant hiatal hernia is fundamental.

In 1949 Wangensteen[15] reported successful treatment of six cases of reflux esophagitis by a three-fourths distal subtotal gastrectomy. The acid-pepsin factor is reduced and the gastric emptying time is shortened by this procedure. The resection must be adequate to reduce the gastric acidity, otherwise the ulcerogenic mechanism will not be relieved.

Vagotomy with pyloroplasty compromises the ulcerogenic mechanism, is less radical, and, if the hiatal hernia is repaired, many cardioesophagectomies may be prevented. All of this can be done through the abdominal approach. If exposure is inadequate the sternal splitting incision described by Wangensteen[13] may be utilized or the xiphoid can be removed[11]. The exposure obtained by either method is excellent and we have used them both with satisfaction. The right crus of the diaphragm and the lower one-third of the esophagus are easily exposed.

Recently Barnes and McElwee[2] presented a different approach to this problem which we have considered as the next logical step. This consists of resection

of the upper stomach and lower esophagus, followed by closure of the upper gastric margin. Continuity is then reestablished by a Roux-Y esophagojejunostomy. In this manner reflux of gastric juice into the esophagus is completely eliminated, unsuspected carcinoma is not left behind[8], and the remaining gastric segment may prevent some of the objectionable sequelae that frequently follow total gastrectomy. Further, the Roux-Y prevents pancreatic esophagitis.

Conclusions

1. The "cardial-sphincter-mechanism" is poorly understood but all agree a closing mechanism exists which determines unidirectional flow. This function is probably a result of the combined activity of the intrinsic and extrinsic mechanisms, consisting of "constrictor cardiae", the action of the right crus of the diaphragm, gravity, the esophageal secretions and the angular junction between the esophagus and stomach.

2. No uniformly satisfactory treatment is available for control of acid peptic esophagitis with stenosis. It is very desirable that the process be treated in its reversible stages before esophageal resection becomes mandatory.

3. The early recognition and immediate surgical treatment of a hiatal hernia with associated refractory esophagitis is of the utmost importance if stenosing esophagitis is to be avoided.

4. Cardioesophagectomy gives unsatisfactory results in the absence of achlorhydria.

5. The results of the cases treated at the Los Angeles County Hospital and presented here do not offer a solution to the surgical treatment of advanced acid peptic esophageal stricture. However, they justify trial of the procedure recommended by Barnes and McElwee[2].

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INTEGRATIVE ESOPHAGOGASTROSCOPY*

A. RAY HUFFORD, M.S., M.D.

Grand Rapids, Mich.

On this particular occasion, the Fifth Annual Postgraduate Gastroenterological Course of the National Gastroenterological Association, it gives me great pleasure to present a topic which, in my opinion, is of considerable importance from a diagnostic standpoint. I sincerely hope that it will stimulate your interest and diagnostic acumen. There are, no doubt, some of you who are already familiar with most of what I have to say, but the prospective may be somewhat unusual and unique.

We are all aware that at intervals in the practice of medicine it is wise to stop and reflect on the accuracy of procedures which may be taken for granted because of their commonplace application. This particular reflection has to deal with most of the practical considerations regarding the integrative use of the modified esophagoscopes and gastroscopes, for safety and acceleration of more positive diagnosis. There are, of course, many practical aspects to be considered in view of the large variety of pathologic conditions in which these scopes are useful as diagnostic instruments.

Like most problems, the solution can only be arrived at step by step after much labor and confusion, but such is true of most all of our medical experiences. As Thomas Huxley[1] once said in an address "On Medical Education", ". . . the rung of a ladder was never meant to rest upon, but only to hold the man's foot long enough to enable him to put the other somewhat higher". This quotation can truly be applied to esophagoscopy and gastroscopy, which has been steadily going up the ladder step by step, though accomplished at times with a great deal of difficulty and hardship. Having made progress it is still important we do not rest upon the present rung.

One of the greatest concerns of all medical men is to detect and treat any and all types of lesions before they have advanced too far. This is especially true of lesions which may be associated with malignancy later on, or primary incipient malignant lesions before they give rise to clinical symptoms of the more advanced type. Guess work in dealing with any esophageal and gastric lesions should be eliminated because of the relatively high incidence of carcinoma. The earlier a lesion is discovered and eradicated, the greater is the productivity of a high salvage rate. The physician charged with the responsibility of advising patients in these matters should realize that earlier cancer may give only presumptive evidence. Only too often the esophagus and stomach are considered to be essentially negative when the roentgenologic examination has not been able

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to depict some definite tangible evidence of disease, or unless bleeding, dysphagia or pain is present. It is unfortunate that the early signs and symptoms of malignancy are so often indistinguishable from discomfort that often occurs during the wear and tear following some indiscretion in eating or drinking, or from nervous tension. For instance a substernal distress or tightness may occur during the act of swallowing too rapidly, boluses of food or liquid that are too hot or too cold, or too large or too irritating. The same can be reproduced by lesser amounts or less irritating foods or drink when infiltration and ulceration is yet early and not marked, however, it is hard for the patient to differentiate. In as much as the esophageal and gastric walls are pliable and therefore tremendously distendible, pain is consequently not an early symptom in these organs. Only by an alertness to the slightest clinical changes and an optimal threshold of suspicion, can we be guided to seek these early lesions by careful radiologic examination and endoscopy when indicated.

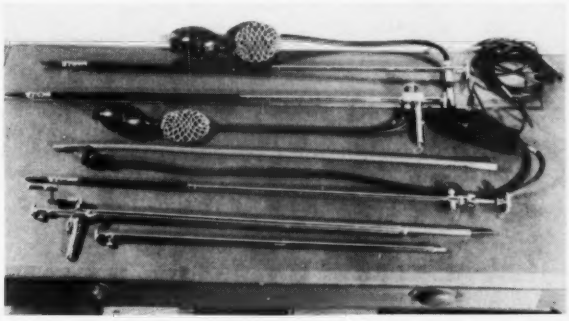

Fig. 1–Instrument table set up for endoscopic examination. The instruments from top (back of table) to bottom are arranged as follows,–Eder light weight standard flexible gastroscope, Eder-Chamberlin Model #400, controlled flexible gastroscope, Drainage tube, Eder-Flexirigid gastroscope and the Eder-Hufford flexible esophagoscope with flexible obturator in place and telescope attached. A lens obturator (for optional use) lays in the foreground. The rheostat and cords are to the right.

Delay in diagnosis of cancer until the last few years has been largely the fault of the patient. Today, however, the patient's responsibility seems to be gradually decreasing through cancer education, while that of the physician actually appears to be increasing. It is quite clear that a completely passive attitude regarding the upper gastrointestinal complaints with negative roentgen findings is no longer tenable. However priceless the roentgen-ray is as a diagnostic instrument, it is an impersonal one and can deceive the gastroenterologist and roentgenologist alike. The basic limitations of a two dimensional shadow given by any body structure may be so altered at times by muscular functions producing artifacts or anomalies otherwise trivial but startling on the film. While the roentgenograms may establish proof of a tangible lesion in approximately 85 per cent of the cases with a definite organic disease, it is doubtful if conclusive diagnostic evidence is furnished by a single or repeat roentgen examina-

tion in much more than 50 per cent of the esophageal and gastric lesions when they are still early and not too far advanced.

With improvement in medical treatment and surgical technic, relative to lesions of the esophagus and stomach, we have come to recognize the importance of early diagnosis in the so-called precancerous lesions as well as in more advanced lesions. In as much as every one of these patients presents a diagnostic problem, it is imperative that every scientific procedure should be employed in the examination to increase the accuracy of the diagnosis and to provide for early and specific treatment. This is a challenge to all physicians and especially to the gastroenterologist.

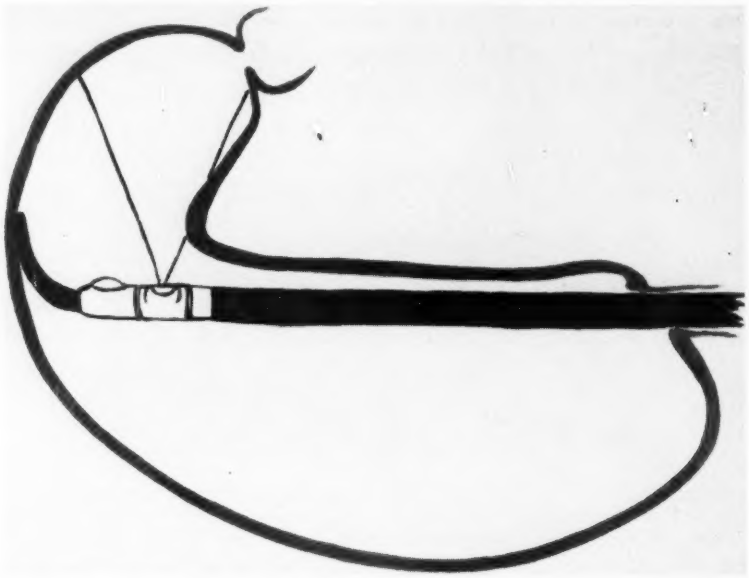

Fig. 2—Diagram of stomach with standard flexible gastroscope *in situ*, at greatest depth of insertion showing angle of vision directed toward the distal end of the antrum. The angulus blocking a portion of the upper visual field creating a blind area along the lesser curvature of the antrum.

We must all be alert to initiate new advances which will alleviate suffering and illness. Since the introduction of the flexible gastroscope by Schindler[2] and Wolf, a new era in gastroenterology was opened because direct inspection of the gastric mucosa was a most useful diagnostic adjunct to aid in supplementing the usual clinical and laboratory procedures, including the roentgenologic examination. The history of gastroscopy as delineated by Schindler[3] and the progress made in the past decade is truly fascinating. A better understanding of gastric pathophysiology has resulted in earlier and more accurate diagnosis. Gastroscopy was fortunate from its inception in having encouragement, counsel and advice of outstanding gastroenterologists, gastric surgeons, and roentgenologists. In my experience painstaking endoscopic examinations have been most gratifying

to all concerned. Schindler et al[4] state that, "more experience in gastroscopy and better diagnostic methods might well reveal a higher incidence of lesions and higher preoperative diagnosis". Surely any nonsurgical exploration of the esophagus and stomach with suspicious clinical and roentgen findings, is a much more desirable procedure than a surgical exploratory laparotomy. Of course the gastroscopist should be endowed with the proper training, knowledge and technic, and should endeavor, at each examination, to properly utilize all the facilities available in order to procure a definite diagnosis.

I shall not document in detail the accomplishments of the many men of science that have made noteworthy contributions to this particular phase of

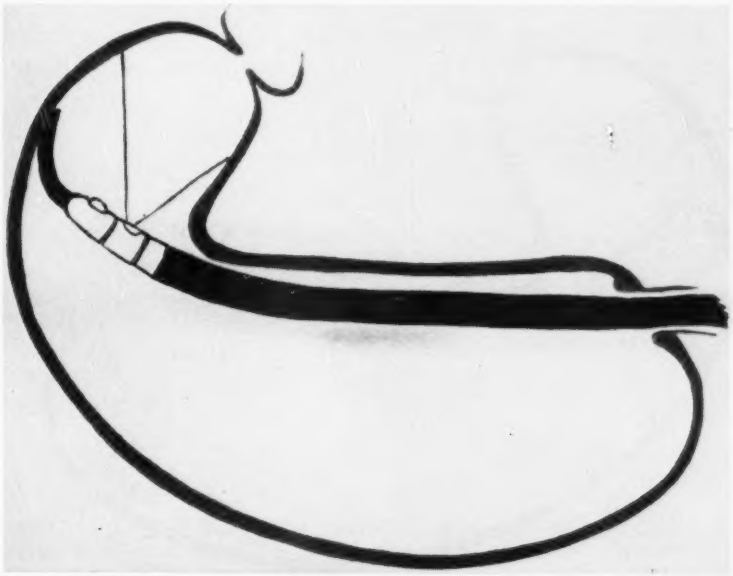

Fig. 3—Diagram of stomach with Eder-Chamberlin controlled flexible, Model #400 gastroscope *in situ* at greatest depth of insertion. Showing angle of vision directed at the antrum and scope flexed sufficiently to avoid interference of angulus to upper visual field. Avoids most all the blind areas along the lesser curvature.

medicine. As a result of extraordinary progress in the development of improved esophagoscopes and gastroscopes in recent years, as well as refinements in technic, endoscopic diagnosis of the upper segment of the gastrointestinal tract has begun to reach a stage of maturity and the wholesome respect of the other specialties. The literature is replete with clinical reports which attest to the usefulness of these diagnostic instruments. The limitations of the endoscopic procedure has been well defined and documented.

Since the introduction of the flexible, closed tipped, optical esophagoscopes in the last few years by Boros[5], Schindler[6] and myself[7,8] a greater interest in esophageal lesions has been manifest by many of the gastroscopists. Esophag-

oscopy which had previously assumed the aspects of a superior surgical approach was no longer a formidable operation. Because of the similarity of preparation and mode of passage, there is a gradually growing tendency for the gastroscopist to use these modified esophagoscopes with ease and safety. It is not only a new innovation to him but a most worthwhile supplementary diagnostic instrument. One might conclude that a kind of endoscopic renaissance has taken place. Previously, in spite of all the clinical knowledge we had of the esophagus, it was sort of a "No Man's Land", and for a long time physiological abberations and pathologic alterations were frequently overlooked until the lesions were well and often far advanced. Even at the present time there is often a lack of understanding in reference to effective methods of diagnosis and treatment.

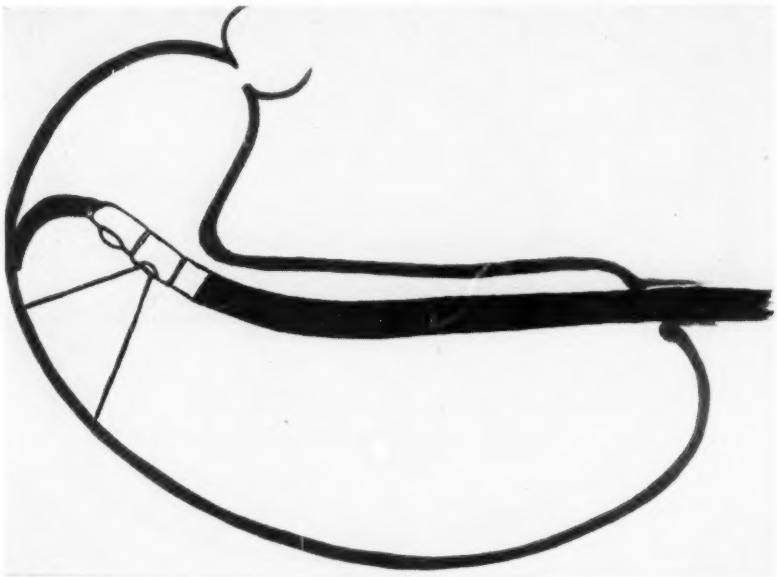

Fig. 4—Diagram of stomach with Eder-Chamberlin controlled flexible, Model #400, gastroscope *in situ* at greatest depth of insertion and extended so angle of vision is directed toward the greater curvature area where tip of standard gastroscope would rest and which area would be a blind spot to it.

Gradually the gastroscopist has become more mindful of the esophagus as a true integral part of the digestive tract through which he must pass the gastroscope blindly and at times with considerable risk, and will come to recognize that this organ is subject to a large variety of organic and functional diseases as well as anomalies of development.

Previous hesitancy of the gastroscopist to employ the esophagoscope was for two main reasons. One was the inherent dangers and disadvantages of passing an open end rigid esophagoscope. The mode of passage and technic was entirely foreign to him. In the second place, esophagoscopy in many large medical centers was, and in some still is, to a large extent dominated by the

endoscopists in the department of Otorhinolaryngology. It has only been in recent years that a relatively few gastroscopists have dared to defy the otorhinolaryngologists and undertake esophagoscopy on their own. Many gastroenterologists who aspired in this field of endeavor in the past have been constrained to forego ambitions in this specialty because of failure and misfortune. The result was that only a limited few were the chosen children in whose hands reposed this important diagnostic method, and for the most part were outside the sphere of gastroenterology.

Since all men and all instruments have definite limitations it is most important to recognize them and to deploy that which we have available so that it can be correlated and integrated for the greatest amount of good and usefulness for which it was intended. It will be the responsibility of the esophagogastroscopist to have the training, experience and possession of the essential

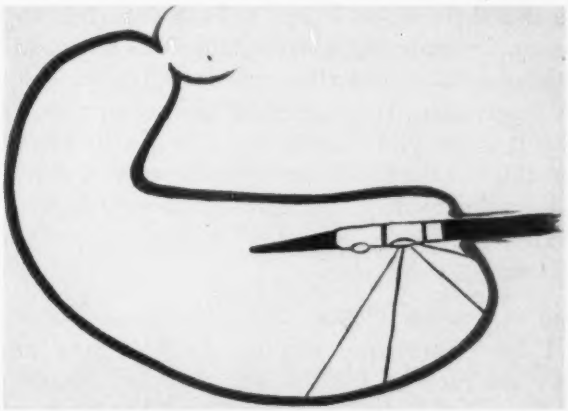

Fig. 5—Diagram of stomach with Eder-Flexirigid gastroscope in position for viewing the fundus. The angle of vision can be moved through an arc of approximately 85 degrees, from prograde to retrograde, permitting excellent inspection of the regions of the fundus not readily viewed by any other scope.

equipment which will enable him to make a complete inspection of the entire esophagus and stomach.

It is apparent that many lesions or conditions affecting the esophagus and cardia is a definite contraindication to the passage of the gastroscope. Suspicious lesions of the esophagus which may give rise to high epigastric or substernal distress, unexplained hematemesis, hiatal hernia with or without esophagitis, erosions or ulceration, constricting lesions and functional disturbances should be inspected through the optical esophagoscope. At times, however, without previous knowledge or warning, the flexible gastroscope may fail to pass the cardia. Various reports in the literature implicates the failure to do so for several reasons. The usual causes of failure from some mechanical blocking by early malignant infiltration in the region of the cardia, paraesophageal hernia, gross deformities of the chest, mediastinum or spine producing marked dis-

tortion and increased angulation of the esophagus just above the diaphragm. At times enlargement of the left lobe of the liver, cysts of the body or tail of pancreas or even pancreatitis may produce interference.

As a general rule I use the Eder-Hufford flexible optical esophagoscope of 8 mm. or 10 mm. diameter, 53 cm. in length for the inspection of the esophagus and cardia if any lesion is suspected that would create a definite hazard to passage of the gastroscope. I also use it in case the lesion in question may be just below the cardia and so situated that it might not only create a definite hazard to the passage of the gastroscope, but might be in such close proximity to the objective lens as to render inspection impossible. The esophagoscope can be guided through the cardia for inspection in the fundus, in which case it becomes an open end rigid gastroscope.

When we are assured from clinical, laboratory, roentgenologic examination or esophagoscopy that there are no lesions or hazards in the esophagus or cardia, then gastroscopy can be undertaken when indicated. All gastric ulcers demonstrated by roentgenological examination or suspected clinically should be gastroscoped for obvious reasons. It is important that when a gastric ulcer is found, to try and assess if it is benign or malignant. If considered benign the patient is usually assured of this but the fact is stressed that careful observation of healing of the ulcer while under medical management is very important. Also careful follow-up observation is equally important to make sure that the ulcer does not recur.

Prudence and experience dictates the selection of endoscopic instruments and technic as I have previously mentioned. It is very important to have available a proper selection of instruments (Fig. 1). For the majority of my gastroscopic examinations I have found the Eder-Chamberlin controlled flexible gastroscope to be superior to the so-called standard flexible gastroscopes (Fig. 2). The optics, field and angle of vision make it an excellent instrument for viewing the greatest amount of gastric mucosa. By means of a control wheel near the ocular, the gastroscopist is able, at will, to flex or extend the distal portion of the flexible section approximately 30 degrees in either direction. This is of particular value when you wish to inspect the large area of the posterior wall which is almost always a blind area by reason that the objective lens is much too close to the mucosa. By extending the control tip to the proper focal distance, all of the mucosa can be brought into view. Likewise the same can be accomplished for viewing the blind area of the greater curvature area opposite the angulus where the tip of a standard gastroscope must come to rest at the greatest depth of insertion, often designated as Position 1 (Fig. 3). Inspection of the antrum is more complete by virtue of the control features because sufficient flexion allows the tip of the scope to be advanced sufficiently into the proximal antrum so that the angle of vision is less impaired by the angulus, thereby permitting a fuller view of the distal antrum and pylorus (Fig. 4). This in itself is worthwhile because of the large number of antral lesions.

If a lesion is suspected in the fundus and not conclusively demonstrated during inspection by any of the other scopes, immediately on withdrawing the scope, it is my practice to insert the Eder-Flexirigid gastroscope. It has a manually controlled objective mirror and a relatively higher magnification than any other scope. The mirror is so pivoted that the field of vision can be swung through an arc of 85 degrees, from prograde to retrograde. In the retrograde position a most satisfactory view of the fundus surrounding the cardia can be obtained (Fig. 5). Inspection of the upper third of the stomach is very important because approximately 15 per cent of benign ulcers and 10 per cent of gastric carcinomas occur there. Aside from the superior ability of the flexirigid gastroscope to inspect fundic lesions through retrograde action, is the magnification which enables one to more carefully scrutinize suspicious areas of gastritis or malignancy, especially the margins of questionable ulcers.

Within the last few years at least two different types of gastric-biopsy instruments have been introduced. From reports of various gastroscopists who have used such instruments, there is a mixed reaction. Some are overly enthusiastic while others are quite skeptical. I have had no personal experience with any of them and do not recommend their use until further trial by those who are already experienced in their use can demonstrate conclusively the procedure is safe and the effort is rewarded with superior diagnostic criteria. We are all aware of the faults of small superficial biopsies. Unless sufficient tissue can be obtained deep enough in the lesion to give the pathologist a chance to make a positive diagnosis, the risk involved is not justified. Whenever a lesion is so questionable in my judgment, either at the first or second gastroscopy, that I feel a biopsy in indicated, I much prefer to refer the patient to the surgeon and have the questionable lesion removed and a real pathological study made of the tissue in question.

In conclusion allow me to summarize briefly. Esophagoscopy and gastroscopy are both well recognized clinical procedures which supplement roentgen examination and usually supply valuable additional information. Clinical experience in the use of the improved types of scopes by well trained and competent gastroenterologists has been sufficient to allow an appraisal of their diagnostic importance. It is not my purpose to compare the virtues of one diagnostic method or instrument with another, but to bring only to general awareness the diagnostic aid of endoscopic methods which, when properly coordinated and integrated for their greatest usefulness, will increase the accuracy of the endoscopic procedure. I believe that it is imperative that the endoscopist should be an esophagogastroscopist with the necessary diagnostic armamentarium at hand which, when used in its proper prospective, either singly or multiply as indicated, will result in more rapid and accurate diagnosis. Prudence and experience dictates the selection of endoscopic instruments and technic. So much depends on the location of the lesion. It is impossible to always achieve our objective when we are confined to the use of any one instrument, for they all have their limitations. The

knowledge of the limitations as well as the particular usefulness of each instrument will produce more fruitful results. It is with this in mind that the subject is presented.

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Discussion

Dr. I. Snapper:—For the diagnosis of an esophageal disease, x-ray examination has for many years been the method of choice. Everybody will agree that with an esophagogastroscope the diagnosis can be often made in an earlier stage and with more accuracy. In older people with coronary insufficiency, however this method of investigation should be used with great discretion because the exertion connected with this procedure makes it a major intervention for coronary patients.

Dr. O. H. Wangensteen:—Gastroscopy and esophagoscopy have an interesting historical background. Kussmaul of Heidelberg, as long ago as 1868, was able to visualize a cancer in the upper esophagus by instrumentation. V. Mikulicz was the first to use the gastroscope in 1881. It was a long, rigid and impractical instrument, which Mikulicz said he had to abandon because of the curvature of the spine. Actually, gastroscopy only became practical with development of the flexible gastroscope by Schindler in 1923. Dr. Hufford's paper traced some of the more recent developments in these technics. It is good to see as much ardent enthusiasm for these agencies of examination as is evidenced in Dr. Hufford's paper.

Earlier today, Dr. Snapper was inquiring concerning the hazard of perforation of the esophagus by instrumentation. In 1935, at a meeting of the American Thoracic Society, I heard Dr. John Alexander say that the mortality of esophagoscopy at Ann Arbor was 10 per cent. I asume that the technic of esophagoscopy done by persons interested in and trained to do it has corrected that situation there. Esophagoscopy in many clinics is largely in the hands of the otolaryngologists. Until very recently, they had no interest in the esophagus *per se*, but only in the instrument they passed into the esophagus. Now, I think, we must all admit this is not good practice. Otolaryngologists, however, are de-

veloping a keener interest in the diseases of the esophagus which the esophagoscope, with the aid of an experienced observer at one end, is intended to uncover. Yet, in our own clinic, a few years ago, it was not uncommon practice to allow the youngest house officer on the otolaryngological staff to schedule cases for esophagoscopy after he had seen it done and was able to recognize the instrument. Perforation of the cervical esophagus opposite the cricopharyngeal muscle occurred far too frequently, leading to correction of the practice of having untrained personnel do the procedure.

A few such perforations concerned patients on the Surgical Service. In consequence, I made it a practice to be very much in evidence when any of our patients were to be esophagoscoped, manifesting great interest in *who* was going to do the procedure; *what anesthetic* was to be employed; where the *Chief* of the Service was, etc. Obviously, a junior resident on otolanryngology found these questions so embarrassing that, the procedure became to be regarded as not the primary spring board for the young house officer in otolanryngology to embark upon his career.

In fact, many patients find esophagoscopy a rather uncomfortable procedure. As some of you know, I have been quite interested in megaesophagus and esophagitis. A few years ago, I became very much interested in having the patients, upon whom I had operated for megaesophagus (esophageal dystonia) reesophagoscoped. I was able to get 100 per cent cooperation from all the patients in the series by promising them a brief, general anesthetic; that there would be no risk in the procedure; and that an experienced esophagoscopist would do it. All this has had a salutary effect in our institution in pointing up the circumstance that the performance of esophagoscopy is not a procedure for a novice.

The same, of course, can be said for other technics of instrument examination. I would like to stress, moreover, the importance of having trained personnel do sigmoidoscopic examinations. Proctoscopy is an examination which anyone who will take the time can do; the same cannot be said of sigmoidoscopy. A patient having such an examination deserves the services of a person trained in the use of the instrument. Otherwise, incomplete examination, as well as unnecessary hazard of perforation of the bowel, are likely to follow.

SURGICAL ASPECTS OF DUODENAL ULCER*

CLARENCE J. BERNE, M.D.

Los Angeles, Calif.

It is my purpose to review the principles involved in the surgical procedures available for the control of the mechanisms that produce duodenal ulcer. An attempt will be made to present these considerations as though they were being submitted to a surgeon for orientation relative to the several technical procedures reasonably applicable, and particularly to familiarize himself with certain clinical and experimental evidence pertinent to those procedures. Such an approach implies the possibility of creating a basis for an attitude favoring individualization in the selection of an operative procedure for a given problem.

The surgeon's approach to these problems involves a critical survey of his patients and the available surgical procedures. Generally, the patients consist of those persons about whom physicians have reached the conclusion that the ulcer disease present is intractable or progressive. There are basic considerations involving such patients that the surgeon must evaluate himself, and at least one of these requires discussion. It is common for the patient to manifest disappointment in the series of physicians he has had on the basis that each has at one time or another stated that the ulcer was cured. This often is closely related to the patient's concept that he is now going to have his ulcer removed. Both of these fallacies can and should be avoided, by his being taught that the day before he originally developed his ulcer he did not have one, and yet the next day an ulcer was present. Further, this was necessarily true of each recurrence, and therefore he must understand that his basic problem was not the ulcer but the mechanism causing it. This concept symbolizes much of our progress in understanding duodenal ulcer. Correlatively, it is clear that surgery limited to removal of the ulcer would be useless, and that the operation to be done must control the ulcerogenic mechanism.

Mechanism of Acid Pepsin Stimulation

Any surgical or medical management of duodenal ulcer must be based upon a clear understanding of the mechanisms that stimulate acid-pepsin secretion by the mucosa of the body of the stomach. At present these are classified as cephalic, antral, intestinal and adrenal. The cephalic phase is considered to involve a neural axis from the frontal lobe to the anterior hypothalmus to the vagus nerves, and provides neurogenic stimulation of the acid-pepsin producing area of the stomach. Less generally appreciated is the fact that this same gastric area is a target organ for hormones arising from the gastric antrum (which produces no acid),

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From the Department of Surgery, University of Southern California.

from the small intestine and from the adrenal cortex. These hormones, especially the antral and adrenal, are potent stimuli for the production of hydrochloric acid, pepsin[1], and mucoprotein. A further product is pepsinogen, which delivered into the blood and excreted by the kidney makes of this gastric target area a gland of internal secretion as well. Urine levels of this pepsinogen quantitatively reflect gastric function. The therapeutic possibilities in the hormonal field also involve recognition of the fact that emotogenic influences generally considered to operate primarily by the vagal pathway alone may, as the result of acute or chronic stress, also operate over the hypothalamic-pituitary-adrenal cortex route[2]. Even the pain of the duodenal ulcer itself probably constitutes a very major stressor which is capable of establishing a self-perpetuating vicious cycle by reason of the resultant adrenal stimulation and by the corticovagal increase in gastric secretion and motor activity with consequent aggravation of the ulcer. This then results in further stimulation of these mechanisms by the resultant pain. In summary, it is evident that acid-pepsin production can be eleminated by destroying either the stimulating mechanisms or the effector acid-pepsin producing area lying between the cardia and the antrum. Further, acid-pepsin secretion can be reduced quantitatively by destruction of one or more of the stimulating mechanisms, or by quantitatively removing acid-pepsin producing gastric mucosa.

Experimental Peptic Ulcer

After consideration of the foregoing, the surgeon should turn to an analytical consideration of the available operative procedures for control of severe duodenal ulcer, which, ideally should offer, without mortality, complete control of the disease with no more than minimal side-effects. The knowledge gained by the experimental laboratories requires review, and should begin with the Mann-Williamson operation which was the first standard operative procedure to produce experimental peptic ulcer[3]. In this procedure, the duodenum carrying its alkaline bile and pancreatic juice, is anastomosed to the lower ileum, and the stomach is then anastomosed to the jejunum. There follows a very high incidence of jejunal peptic ulceration. These animals acquire significant nutritional difficulties because of the low deviation of the digestive juices into the ileum. This procedure was the first to solidly establish the importance of the acid factor. One frequently overlooked phase of this work was Mann's study of the effect of producing an hourglass constriction in the middle of the stomach in Mann-Williamson dogs[4]. Such a constriction markedly decreased the propulsive force of gastric emptying, and eliminated the occurrence of jejunal ulcer. This correlated with previous reports that is a pedicled jejunal patch transplant was placed in the wall of the stomach of a Mann-Williamson dog, and a gastrojejunostomy then done, jejunal ulceration would occur opposite the anastomotic stoma, but the transplant exposed as it was, to the gastric lumen, would not ulcerate[5]. Further progress in the experimental production of canine duodenal ulcer occurred as a result of Wangensteen's use of histamine in beeswax[6]. This

specific stimulus to the gastric acid and pepsin producing cells consistently produces duodenal ulcer in dogs who possess no other recognizable physiological disturbance. Wangensteen states that any operation which protects animals against histamine induced ulcer will also protect humans, and his procedure is certainly an "acid test". The stimulus, however, is not a physiological one. On theoretical grounds, surgery that eliminated all the physiological acid stimulating mechanisms but preserved the acid producing area of the stomach would fail completely to "pass the test". Dragstedt[7] has more recently designed an operative procedure on dogs consisting of transposition of the gastric antrum to the colon, as a pouch, completed by gastrojejunostomy. There results a sustained hypersecretion of antral hormone, with consistent production of jejunal ulcer. If, however, the stomach anastomosis be made with duodenum instead of jejunum, the ulcerogenic mechanism is relatively incapable of producing ulcer. This fact emphasizes that whenever the stomach is anastomosed to the jejunum the avoidance of subsequent ulceration requires greater concomitant suppression of the ulcerogenic mechanism than if the stomach be anastomosed to the duodenum. It is known that in the human, removal of the antrum is by itself inadequate to control the ulcerogenic mechanism. As has been clearly shown by McKittrick and associates[8], however, if subtotal gastric resection and gastrojejunostomy is done, but some antral mucosa near the pylorus is left *in situ,* there results a level of gastric acid secretion that is much higher than when the whole antrum is removed. A more recent laboratory procedure, by Harkins and associates[9], consists of division of the stomach just below the cardial cuff. The upper end of the stomach is closed and the stomach, with vagi intact, is connected to the duodenum by a segment of jejunum. Such dogs have all the acid stimulating mechanisms intact. The relative importance of each can then be measured by eliminating the antrum, or the vagi, or both. Study of such preparations clearly shows that the antral hormone of dogs exceeds the vagus as an acid stimulating mechanism, but that elimination of both gives almost complete protection against jejunal ulcer which occurs regularly in a severe form if both mechanisms are intact. The foregoing gives some few indications of the progress of study in the laboratory field. Other laboratory findings will be cited in relation to specific operations in the human.

Subtotal Gastric Resection

The operative treatment of duodenal ulcer had become relatively standardized by 1945, the procedure of choice being three-quarter resection of the stomach completed by a short loop gastrojejunostomy. Further criteria laid down included division of the left gastric artery with division of the lesser curvature above this level and division of the greater curvature to a level at least above the lowest short gastric branches to the spleen. Distally, all of the antrum and pyloric ring required excision. The ulcer need not be removed. It is evident that the objective in this procedure is subtotal resection of the acid-pepsin producing target area, and elimination of the antral acid stimulating

mechanism. Further, resection of the acid producing area must be so extensive that the anastomosis of the gastric stump to the acid susceptible jejunum is usually not followed by jejunal ulcer. In 1953, most surgeons consider this procedure the operation of choice. Its shortcomings are well identified. Cole[10] reported a mortality rate of 5.8 per cent, Moore and associates[11], 2.86 per cent, and Ransom and associates[12], 6.1 per cent. There are series with both higher and lower mortality figures. Frequently, however, the results of the procedure are reported only in terms of the status of the survivors, which has led us to believe that unless the deaths are included in the results of the operation, the figures should be in white letters on black paper. The next most serious poor result to follow this procedure is gastrojejunal ulcer. Ransom[12] reports its incidence as 9.4 per cent, while Colp[13] places it as 4.8 per cent. The frequency of serious nutritional difficulty and severe dumping syndrome is difficult to state as the reports vary widely. In as forthright an analysis as one can find, Moore[11] reported unsatisfactory results in 23.9 per cent of cases after 155 subtotal gastrectomies done on the surgical services of the Massachusetts General Hospital. It would seem reasonable that the surgeons who prefer this operation do so not because of satisfaction with it, but only because they believe it to be the best available.

Vagotomy

At just about the time that subtotal gastric resection became standardized, Dragstedt[14] reported his experience with the operation of vagotomy. Although in the eight years that have passed many vagotomies have been done, the ultimate status of procedure has not been determined. So far as is known vagotomy does no harm[15]. General agreement exists that regeneration does not occur. A real problem with the operation of vagotomy is the fact that, in a significant percentage of cases, the nerves are not anatomically arranged to make complete vagotomy easily accomplished. Therefore, a high percentage of successes is dependent upon the degree of painstaking care and upon the zeal which the surgeon exercises when he prepares himself in the dissecting room, and again when he carries out the operative procedure. Careful study of Grimson's[16] "Critique of the Committee Report" is mandatory for any student of duodenal ulcer disease. Dragstedt clearly established that complete vagotomy abolishes the hypersecretion of acid in the fasting stomach of humans affected with duodenal ulcer. Further elaboration of this effect has made possible the concept that vagotomy abolishes the so-called cephalic phase of acid-pepsin secretion. Less has been recorded relative to the role played by the elimination of gastric hypertonus, which is potentially a very important factor in the production of duodenal ulcer. An observant clinician is impressed with the tension factors in duodenal ulcer symptomatology. Also, in this regard it is reasonable to recall the studies of Mann which demonstrated the failure of jejunal ulcer to develop in Mann-Williamson dogs when an hour-glass stomach was created, eliminating the propulsive force with which the gastric content was ejected into the jejunum.

Further, it must be emphasized that in the preoccupation on the acid-pepsin factor in duodenal ulcer, it is seldom pointed out that if this were the sole factor, one whould expect a diffuse ulceration of the entire circumference of the duodenal mucosa by reason of the diffuse application of acid-pepsin; whereas the opposite is true: the ulcer usually involves only a relatively small area, while the remainder of the mucosa is intact. This strongly suggests that a jet factor is operative. Vagotomy, by producing a hypotonic stomach, accomplishes an effect qualitatively similar to the hour-glass stomach in Mann-Williamson dogs. One other feature of postvagotomy gastric hypotonus requires consideration. Grossman, Robertson and Ivy[17] reported that on the basis of their experimental studies, mechanical distention of the antrum was an important stimulus to the formation of the antral hormone. In the vagotomized stomach, inherently poorly drained, antral distention is excessive, but where drainage is provided, the gastric hypotonus determines a marked lowering of antral pressure as compared to the preoperative state. In clinical practice, vagotomy has now come to be regularly complemented by a drainage procedure.

Present day surgical treatment of duodenal ulcer aimed primarily at elimination of the cephalic phase of gastric secretion consists of vagotomy and gastrojejunostomy or pyloroplasty. The former procedure has been extensively studied and reported by Dragstedt[14], Grimson[18] and Crile[19]. There are many conflicting reports available. One series of cases, however, all done within one year and followed for five years, was reported from the University of Michigan by Ransom and associates[12]. In this series approximately half were treated by vagotomy and gastrojejunostomy, and half by subtotal gastric resection. In each group, approximately 85 per cent of the survivors were reported as having obtained satisfactory results. There was no operative mortality in the vagotomy-gastrojejunostomy group. In the subtotal resection group, the operative mortality was 6.1 per cent. The recurrence rate was 9.4 per cent in the subtotal resection group and 4.7 per cent in the vagotomy group. Practically all the recurrences were manifested within two years. There was no correlation between the recurrence of ulceration and the insulin test. Crile[20] has indicated the desirable modifications of the usual gastrojejunostomy when used with vagotomy. There are liabilities connected with the use of gastrojejunostomy. The early postoperative technical complications of gastrojejunostomy, the possibilities of dumping syndrome, and of jejunal ulcer are all inherent as in the gastrojejunostomy following subtotal resection. Also, Heidenhain pouch studies in dogs have indicated that gastrojejunostomy increases gastric secretion[21]. Absolute restriction of drainage to the duodenal route with its inherent capitalization on the greater ulcer resistance of the duodenal mucosa, the better stimulation of the pancreatic juice and other anthelones by reason of all the food passing through the duodenum, and the possibility of additional benefits by elimination of the jet factor by the use of pyloroplasty, has led some clinics to prefer the Heineke-Mikulicz procedure to gastrojejunostomy. In the past gastrojejunostomy and pyloroplasty have each produced good but not acceptable results when used

alone in the treatment of duodenal ulcer, but it is difficult to evaluate their respective contribution to vagotomy on this basis. Weinberg[22] reports 770 cases treated by vagotomy since 1946. In the first 83 only vagotomy was done, in the next 235 cases vagotomy and gastrojejunostomy was done, and in the last 452 cases vagotomy and pyloroplasty of the Heineke-Mikulicz type was done using but one row of sutures for the plastic closure. The mortality rate was .52 per cent. Weinberg has been increasingly satisfied with the pyloroplasty procedure. In summary, it is obvious that more experience is necessary to determine the value of vagotomy, although after eight years it is solidly entrenched in many clinics. Criteria for the selection of cases for this procedure, based on the characteristics of the ulcerogenic mechanism in a given patient are particularly to be desired. Its flexibility by reason of the various possible complimentary procedures makes it technically applicable to nearly all cases. Its proponents find difficulty in understanding how some strongly negativistic attitudes toward the procedure can be based on unbiased scrutiny of the record.

Partial Gastrectomy and Vagotomy

Complementary vagotomy is being evaluated when applied to hemigastrectomy and gastrojejunostomy. Farmer and Smithwick[23] have enthusiastically reported extensive studies. Such a procedure eliminates the cephalic and antral phases of acid stimulation and preserves gastric reservoir function to the maximal degree consistent with ablation of the antrum. Their extremely careful studies indicate a consistent marked reduction of acid secretion, more than with classical subtotal resection. Side-effects such as dumping syndrome are less, presumably because of the larger gastric pouch. Their clinical results were better than with any other procedure with which they had experience. Hemigastrectomy with gastroduodenostomy and vagotomy is logically possible as another field of study.

Gastroduodenostomy following about two-thirds gastric resection with complementary vagotomy has been reported by Fallis[24] who has used it since 1946. He is very much gratified with the results. This procedure possesses all the desirable features of gastroduodenal continuity, eliminates cephalic and antral stimulation and removes a significant area of acid secreting mucosa. Since the antral mucosa extends upward along the lesser curvature, complete excision is assured by the Shoemaker type of gastrectomy used by Fallis. On the basis of all the various factors cited previously in this discussion, this procedure has much experimental evidence to commend it when local conditions make it technically applicable.

Subtotal resection combined with vagotomy has been reported by Colp[13] and associates. Two sizable groups of patients were treated by subtotal resection with vagotomy added in one group. In the nonvagotomy group, the incidence of gastrojejunal ulcer was about 4.5 per cent. The group with vagotomy did not develop any gastrojejunal ulcers. This operation obviously represents the maximum feasible surgical attack on the ulcerogenic mechanism when done

as a primary procedure and the evidence suggests that it constitutes a combined procedure capable of practically eliminating jejunal ulcer in the human. The patient, however, possesses the objectionable small gastric pouch. It has been stated by some that a combination of vagotomy and resection burdens the patient with the undesirable effect of each procedure and because the results of subtotal resection are acceptable, vagotomy should not be done. In this regard Colp observed prolonged moderate diarrhea in 7 per cent of this vagotomy subtotal resection group, and no other side-effects attributable to the vagotomy. Should further experience verify the foregoing, a 7 per cent incidence of moderate diarrhea in exchange for elimination of a 4.5 per cent incidence of jejunal ulcer should be expected.

Experience with vagotomy in the management of postresection gastrojejunal ulcer is sufficiently favorable to justify most surgeons in recommending it. Reports of good results vary from 50 to 70 per cent as compared to Colp's report, showing its much greater effect in preventing the formation of jejunal ulcer. It is immediately obvious that until the statistics change, the procedure appears to be more effective in preventing jejunal ulcer than in curing it. The reasons for this discrepancy are not clear. One is justified in wondering whether or not the pancreatic juice is a factor. Once acid-pepsin activity initiates the jejunal ulceration, the granulating base is at least intermittently flooded with pancreatic juice. Certainly all surgeons are aware of the much more vicious behavior of a duodenal fistula as compared to that of a gastric fistula. At least the discrepancy may be related to the fact that the enzymatic environment of gastrojejunal ulcer is much more complex than is that of duodenal ulcer, just as for the same reasons, but to a much lesser extent, duodenal ulcer has a more complex enzymatic environment than gastric ulcer.

Subtotal Resection With Gastroduodenal Continuity

Aside from vagotomy, one other trend has characterized surgical investigation of duodenal ulcer in recent years. This is based on the desire to eliminate the side-effects of gastrojejunostomy, particularly the dumping syndrome and nutritional deficiency. An answer has been sought in procedures that maintain gastroduodenal continuity. Moore and Harkins[25] have reported an extensive series of cases of duodenal ulcer treated in this manner. Approximately 70 per cent gastric resections were done, proven by measurement. Follow-up studies on such series should establish the position of this Billroth I procedure when carried out in this manner.

Another study aimed at preservation of gastroduodenal continuity is that by Wangensteen[26], who has reported his work with segmental resection of the stomach. Since this procedure preserves the antrum and removes 85 per cent of the acid bearing area, it preserves all the stimulating mechanisms but removes the effector acid producing area. It is strictly unique from a physiological standpoint. It preserves gastroduodenal continuity, and by leaving the doudenal ulcer

in situ, eliminates the morbidity and mortality inherent in any direct attack on the ulcer itself. Experience with the procedure has developed the conviction that removal of the ulcer is entirely unnecessary. The ulcer control seems as good or better than with the Billroth II type of three-quarter resection. Reduction in side-effects seems to have been obtained.

The author has carried out a procedure which consists of vagotomy, pyloroplasty and a large wedge resection of the body of the stomach. The ulcer is left in place, gastroduodenal continuity is preserved, the effects of vagotomy and pyloroplasty are obtained, the acid-pepsin producing membrane is considerably reduced in area, and a moderate gastric capacity preserves the reservoir function. The latter feature is conducive to creating a situation in which the material entering the duodenum is much more like chyme; whereas, after subtotal resection, jejunitis is more likely to result, for the swallowed food presents wide variations in osmotic, thermal, and physical characteristics unless the diet is rigidly managed. All this involves the assumption of a basic concept that less drastic anti-ulcerogenic effects are necessary to cure duodenal ulcer than to prevent jejunal ulcer.

Choice of Operation

With the foregoing orientation, what may be the surgeon's conclusions in selecting a procedure, assuming that he is totally disinterested in carrying out a study of any particular procedure but is trying to select the best procedure for a given case? In the aged with complicating medical problems, subtotal resection should be avoided, and preference should be given to vagotomy and pyloroplasty. When an extensive duodenal ulcer is found, with very active inflammatory reaction around it, vagotomy and gastrojejunostomy is clearly indicated. In the good risk patient with a large, deep duodenal crater indicative of transmural destruction, it has seemed that the pathological factors of extensive loss of substance, fibrosis, and pancreatic involvement are tremendous handicaps to any operation preserving gastroduodenal continuity. Here an exclusion operation is preferable with removal of all the antral mucosa, if the ulcer is near the pylorus and completed by subtotal resection with gastrojejunostomy. With only mural involvement and an ulcer near the pylorus, our tendency is to carry out a Billroth I type of procedure, leaving a gastric pouch large enough for an anastomosis without any tension and then doing a complementary vagotomy. For the average case, where there is mucosal and some mural involvement, vagotomy and pyloroplasty is preferred, since the problem is primarily that controlling the ulcerogenic mechanism. The almost complete elimination of mortality, the elimination of gastrojejunal ulcer, and the relative absence of side-effects make this position tenable. In this group of patients there are those instances where the patient is so strongly prejudiced in favor of subtotal resection as a result of advice given by others that it seems better to carry out that procedure. Also, the occasional patient with a post-bulbar ulcer is considered

to be best treated by a Billroth II procedure. This is believed desirable because such a lesion is so near the papilla of Vater that the acid-pepsin factor is probably mixed with a pancreatic enzyme factor. In addition, several other anatomical factors should be given strong consideration. If vagotomy and pyloroplasty are elected, but the surgeon is quite dissatisfied with the anatomical situation after dissecting the vagi, and believes it very possible that an incomplete vagotomy has been accomplished, it is desirable to complete the procedure by some type of subtotal resection. A second anatomical factor is the patient's physical habitus. In a John Bull type, with a small high lying transverse stomach, three-quarter resection is a much more difficult operation to accomplish than in an Uncle Sam type. In the Uncle Sam type, three-quarter resection is a relative simple problem. While these latter factors may not dictate the decision, they may well condition significantly the type of laparotomy incision made as well as the procedure selected. In our opinion, the weight of experimental evidence suggests that in the future, a conservative Billroth I resection, including removal of the lesser curvature, with vagotomy, may become the physiological procedure of choice when the pathological status of the duodenal lesion is favorable for such a procedure.

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Discussion

Dr. I. Snapper:—As a physician I am sad to testify that the conservative treatment of gastric or duodenal ulcer in ward patients is extremely unsatisfactory. A follow-up examination of patients with peptic ulcer observed in the course of ten years in the wards always reveals that only very few are doing well. This does not hold true of patients in private practice.

If a patient can put his ulcer in the center of his existence, if he can really live for and around his ulcer, then very often the complaints are few and far between.

Although subtotal gastrectomy has made life tolerable for many ulcer patients, the surgeons are evidently still searching for a satisfactory surgical solution of the problem of the refractory peptic ulcer.

Before World War II in Europe many surgeons performed a Billroth II; but some diehards stuck to Billroth I. In this country subtotal gastrectomy with Billroth II was for many years the popular procedure. But after what we heard today resection-pyloroplasty and Billroth I are evidently coming back.

CONSERVATIVE RESECTION FOR GASTRIC ULCER*

HERBERT J. MOVIUS II, M.D.†
ANGELO E. Da GRADI, M.D.†
and
JOSEPH A. WEINBERG, M.D.†
Long Beach, Calif.

Local excision of gastric ulcer by wedge or segmental resection combined with pyloroplasty or gastrojejunostomy has been practiced at the Veterans Administration Hospital, Long Beach, Calif., for over five years. A report on the first 32 cases from this hospital was published in 1951[1]. At that time a review of the results indicated that the procedure was superior to extensive gastric resection, and that continued use of the procedure was warranted. The present report deals with the further follow-up of the 32 cases, and adds another 42 cases.

Surgical removal of the gastric ulcer by means of a wedge resection is not new. Walton[2], in 1935, published his observations on 310 patients treated with wedge resection and gastrojejunostomy. The mortality for the group was 4.2 per cent and the cures were reported as 88 per cent. Balfour and his associates[3] reported a study of 1,202 cases, 574 of them with gastric drainage and the remainder with resection alone. The mortality rate was 3.8 per cent and 82.7 per cent were described as cured or much improved.

While subtotal gastric resection is, from a general viewpoint, a fairly satisfactory procedure for the treatment of benign gastric ulcer, it has some undesirable features that may be overcome by local resection. It is difficult to perform and introduces hazardous technical difficulties in high lying ulcers particularly. The end-results leave much to be desired regarding gain in weight, freedom from symptoms of the "dumping syndrome", jejunal ulceration and operative mortality. Furthermore, it would seem obvious that a better procedure is one in which the patient retains most of the stomach.

The principal objection to subtotal gastric resection as it is performed for benign gastric ulcer which is suspected of being malignant is that it is too limited if malignancy is present, and it is too radical if malignancy is not present. Gastric resection for malignancy demands a thorough extensive resection of the regional lymphatics and the removal of almost all if not all of the stomach. To do less is to do less than is necessary in an operation for cancer, and to do more is to do more than is necessary in an operation for benign ulcer.

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†From the Surgical and Medical Services of the Veterans Administration Hospital, Long Beach, Calif.

One of the reasons for dissatisfaction with local resection of the ulcer in the past was the tendency for ulcer to reform in the stomach in some cases, about 50 per cent according to Eusterman and Balfour[4]. It is being accepted with increasing frequency that the basic diathesis in gastric ulcer is different from that in duodenal ulcer. The older age of the patients in most cases, the relatively lower secretory activity in the stomach, and the difference regarding emotional factors support this view. There is, however, sufficient evidence to make it clear that gastric ulcer is not entirely a local disease. The association of gastric erosion, ulceration and hemorrhage with intracranial pathology is well documented[5]. Porter[6] and his associates have described the effect of anterior and posterior thalamic lesions on the secretion of gastric acid, and the neural and humeral pathways through which the secretory response is motivated. Because of the implication of the vagus nerve pathways in this response, and because of the protection which it offers against stomal ulcer in which gastroenterostomy is the adjunctive procedure, vagotomy has been added to the local resection of the ulcer in most of our cases.

A study of 74 patients who have had local resection of the ulcer with or without associated procedures is the basis for this report. There were 70 men and four women. The ages ranged from 26 years to 71 years with the highest incidence occurring in the sixth decade.

Gastroscopic examinations were made on 53 patients. Table I summarizes the accuracy of the gastroscopic observations, both in making the diagnosis of ulceration and in determining the benignancy or malignancy of the lesions.

TABLE I

GASTROSCOPIC FINDINGS IN 53 PATIENTS WITH PROVED GASTRIC ULCER

Benign ulcer diagnosed correctly	34
Benign ulcer diagnosed as carcinoma	8
Failure to visualize ulcer	11

Gastrointestinal x-ray examinations were made on 72 of 74 patients. Two patients were not x-rayed at the time of admission for surgery because of hemorrhage. Both of these patients, however, had shown roentgenologic evidence of ulceration in previous examinations. Table II, which gives the roentgenologic interpretations, shows that x-ray examination is more reliable for diagnosing the existing lesion in this series.

TABLE II

ROENTGENOLOGIC FINDINGS IN 72 PATIENTS WITH PROVED GASTRIC ULCER

Benign ulcer diagnosed correctly	64
Benign ulcer diagnosed as carcinoma	2
Failure to reveal ulcer	6

Gastric analysis was carried out in 65 patients, using the standard histamine technic. The results are shown in Table III. Anacidity was considered to exist

when the pH remained over 6.5, a pH of 6.5 to 2 was considered to be a state of hypoacidity, a pH of 2.0 to 1.5 was considered as normal, and a pH of less than 1.5 was interpreted as hyperacidity.

TABLE III

PREOPERATIVE ACID VALUES IN 65 CASES

Anacidity pH> 6.5	Hypoacidity pH 2.0-6.5	Normal pH 1.5-2.0	Hyperacidity <pH 1.5
10	13	25	17

The types of operations regarding the association of wedge resection with other procedures is as follows:

Wedge resection alone	2
Wedge resection and vagotomy	8
Wedge resection and pyloroplasty	11
Wedge resection, pyloroplasty, and vagotomy	46
Wedge resection, gastrojejunostomy and vagotomy	7

The combination of wedge resection, vagotomy and pyloroplasty, which was used in a great majority of the cases is the preferred procedure. The wedge excision removes the ulcer with a wide margin of gastric tissue; the vagotomy is used as a protection against the tendency to recurrence of ulceration, and the pyloroplasty facilitates emptying of the stomach without interrupting the continuity between the stomach and duodenum.

The determination of whether or not surgery should be performed in a given case is made at a medical-surgical conference after the patient has been examined and his condition evaluated on the medical gastroenterology service.

Only a general description of the surgical procedure will be given here. A transverse abdominal incision is made in the mid-portion of the upper abdomen. Both rectus muscles are divided. After a careful abdominal exploration is made and the diagnosis in confirmed, the vagotomy is performed. A generous wedge resection is then made, including the ulcer with at least a two centimeter margin of gastric tissue. The excised specimen is delivered to the pathologist for examination of a frozen section from any area which may be under direct suspicion of malignancy. The defect in the stomach is closed while the surgeon awaits the report of the microscopic examination. A gastric emptying procedure is then performed, usually a pyloroplasty of the Heinecke-Mikulicz type with closure with a single row of interrupted fine cotton sutures. If the pathologist finds that the lesion is carcinomatous, the attack is changed, and a radical subtotal or total gastrectomy is performed. If evidence of malignancy is not found in the frozen section, the pathologist makes serial paraffin sections from the ulcer and if carcinoma is found in these sections a day or two after surgery the patient is operated on again after several days, at which time a radical resection with

inclusion of the regional lymphatics is performed. As mentioned before, this is one of the great advantages of local resection. The one patient who returned for a radical resection after evidence of carcinoma was found in the paraffin sections has been followed 15 months without evidence of recurrence of malignancy.

Clinical Results

The patients in this study have been followed by examination and questionnaire for periods of six months to five and one-half years. All were studied by x-ray and gastroscopy during the follow-up if there were symptoms suggestive of recurrence of ulceration. Because of transient habits of a group of individuals in a seaport community, 15 of the patients have been lost to follow-up at this time. Some of these were followed for a year or two before moving. These presented no evidence of ulceration when they were examined last. This much is known. The patients whose residence is not known are not receiving compensation from the government, nor have they been in a Veterans hospital since leaving here. There remained 59 patients on whom the follow-up study is complete.

There have been no surgical fatalities in the 74 patients.

Three of the 59 patients have died since the operation. One succumbed to severe homologous serum hepatitis which was presumably transmitted by the blood transfusions for his shock status from hemorrhage prior to his operation.

One patient died as the result of a carcinoma originating in the mid-portion of the esophagus.

The third death was due to luetic cardiac disease two and one-half years postoperatively. Autopsy was performed in all three of these cases and none showed evidence of recurrence of ulcer or other gastric disease.

There have been two possible cases of recurrent gastric ulceration, one diagnosed only on gastroscopy. This lesion was apparently superficial and healed rapidly on a medical regimen. The other was diagnosed by gastroscopy and x-ray. A second wedge resection and vagotomy was performed. Vagotomy had not been included in either of the cases at the first operation. It is not possible to state with certainty from the x-ray examinations whether or not duodenal ulcer occurred postoperatively in those patients with pyloroplasty for the reason that pyloroplasty deforms the duodenum sufficiently to make x-ray interpretation difficult in some cases. No ulcer craters were seen, however, and in no case did the roentgenologist believe that the duodenal deformity was due to an ulcer.

Retarded gastric emptying has been looked for in all cases, and was found to exist in five patients. There was still some barium in the stomach in six hours in all five of the cases, but there was no retention after 24 hours. Symptoms of fullness and mild discomfort after eating were suggestive of retention in these five. Three of them are working regularly, they have no pain, they have gained weight since surgery and express complete satisfaction with the operation. The

fourth patient takes urecholine occasionally and feels that he must limit his work to part time. The fifth patient had sufficient obstructive symptoms to warrant a second operation at which time a large atonic stomach was found. The pyloric canal was more than ample but the stomach failed to empty because of atonicity. A dependent gastrojejunostomy was performed which has given good symptomatic relief to the present. All five had the operation of wedge resection, vagotomy, and pyloroplasty.

Diarrhea has been present at intervals in three of the patients. In one patient it has been associated with weakness that limits his activities to part time work. The other two are not particularly disturbed, have not lost weight and are working regularly.

Weakness, perspiration, and a feeling of faintness coming on after meals have been noted in two patients. One of the patients is dissatisfied with his operation because of this disturbance. The other has been only slightly bothered and is working regularly. His episodes occur less frequently now than they did earlier.

Thirty-six of the 56 patients are working full time. Twelve are retired, four are working part time, and four state that they feel unable to work although careful questioning and examination in three of these fails to disclose an adequate reason.

With few exceptions, the patients are enjoying a regular full diet. One patient prefers a bland diet, and another controls hypoglycemia-like reactions with a high protein and low carbohydrate diet. Over half of the patients have gained weight since operation, and less than one-third are below what they consider to be normal weight.

One of the most significant criteria as far as the patient himself is concerned is his own opinion of what the operation has accomplished in respect to his feeling of well being. In this respect 53 of the 56 patients questioned expressed complete satisfaction. Two patients chose to withhold comment for a later time, and one patient expressed unqualified dissatisfaction because of epigastric distress and hypoglycemia-like attacks. This patient works regularly, is on a general, unprescribed diet, and has no evidence of peptic ulcer by x-ray examination or gastroscopy.

Comment

The experience thus far with local resection of the benign gastric ulcer has been highly satisfactory. This procedure, which in most of the cases has consisted of wedge resection, vagotomy and pyloroplasty, has been associated with only two possible recurrences of ulcer. In neither of these cases had a vagotomy been performed. There had been no recognizable nutritional disturbances. The sequelae of retention, diarrhea and hypoglycemia-like symptoms have been unusual occurrences. What is most important is the fact that patients operated chiefly because of the possibility of malignancy have been spared subtotal resections which would in no way contribute further to the safety against cancer in

the cases of benign ulcer, and which would be inadequate as ordinarily performed for benign lesions if cancer was found to be present.

Vagotomy is considered to be an indicated adjunctive procedure with wedge resection because of past experiences of recurrence of ulceration in cases in which wedge resection alone was performed. At the same time we recognize that gastric and duodenal ulcer are probably different entities and that vagotomy may be less indicated in the former than in the latter.

Pyloroplasty is indicated to facilitate gastric emptying which tends to be delayed in both wedge resection and vagotomy. It is preferred to gastrojejunostomy because of the maintenance of direct continuity between the stomach and duodenum, the low incidence of surgical complications, the elimination of the possibility of stomal ulcer and the simplicity of the technic. Gastrojejunostomy is reserved for the cases of large atonic stomachs and those with stenosis of the duodenum in which it would be difficult to perform a satisfactory pyloroplasty.

We are aware of the reports of unsatisfactory results in some cases in the past, but our experience up to the present time indicates that the combination of wedge resection, vagotomy and a gastric emptying procedure, preferably pyloroplasty, will reduce the number of unsatisfactory results to an acceptably low incidence.

Summary

1. Seventy-four patients with gastric ulcer have had local excision of the ulcer, usually combined with vagotomy and an emptying procedure.

2. The results of roentgenography, gastroscopy, and gastric analysis are tabulated.

3. There were no operative deaths.

4. Fifty-nine patients have been followed for six months to five and one-half years. There have been two recurrent ulcers. Retention, diarrhea, and hypoglycemia like reactions have been infrequent sequelae. A majority of the patients have gained weight, are eating a regular diet, and are working full time. Fifty-six of the 59 express complete satisfaction with the operation.

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CONSERVATIVE SURGICAL TREATMENT IN MASSIVE GASTRODUODENAL HEMORRHAGE

TIMOTHY A. LAMPHIER, M.D.

Boston, Mass.

and

WILLIAM WICKMAN, M.D.

Miami, Fla.

The problem of treating massive upper gastrointestinal bleeding is frequently difficult, and the decision as to either conservative medical treatment or surgery is most trying. When replacement of whole blood cannot equal its loss through an ulcer bed and when there is no evidence of cessation or "slowing of" active bleeding, surgery is imperative. These patients are notoriously poor candidates for surgery, and the resultant morbidity and mortality rates are extremely high.

Approximately 9 patients out of 10, who hemorrhage from the upper gastrointestinal tract, can be treated medically by bed-rest, frequent blood replenishment, sedatives, antacids, a specific dietary regimen, etc. The degree of hemorrhage in the one remaining patient is so massive that one must subject him to early or immediate operation. Therefore, one operates on only those patients who would not recover by conservative medical therapy. Certain established rules must be followed in order to make a decision for immediate operation. In the first place, we must be absolutely certain that we are dealing with a condition that can be remedied by surgery. In approximately 80 per cent of these cases we can be almost certain that the cause of the hemorrhage is a peptic ulcer. Bleeding from esophageal varices, secondary to portal hypertension, must have been eliminated. No less important is the elimination of a blood dyscrasia as the source of hemorrhage. Occasionally, massive bleeding will be caused by polyposis of the stomach, or carcinoma, or a leiomyoma, and these causes will necessitate operative intervention as a life-saving measure. Other important factors to be considered when surgery is being contemplated is a generous and adequate reserve and supply of blood, a competent anesthetist, a qualified surgeon, and adequate assistance.

There is no question that the best type of operation for massive hemorrhage due to a peptic ulcer, uncontrollable by medical means, is immediate subtotal gastrectomy with removal of the distal two-thirds of the stomach, including the pylorus and that portion of the stomach or duodenum bearing the ulcer. This procedure is followed by the re-establishment of bowel continuity by means of an anterior or posterior Hoffmeister gastrojejunostomy. The situation will occasionally be encountered, however, wherein the carrying out of this ideal procedure will entail a considerable risk to the patient because of his poor general condition or because of the unfavorable site of the bleeding ulcer. In these

cases, a conservative plan of surgical attack may be the wiser approach to the problem. When the ulcer presents on the anterior surface of the stomach or duodenum or when the gastric ulcer does not lie too high on the lesser curvature, subtotal gastrectomy with removal of the ulcer is safely accomplished. When the ulcer is on the posterior surface of the duodenum, however, and is bleeding directly from the pancreaticoduodenal artery, frequently the additional risk of attempting to remove the ulcer is too formidable a procedure for such a patient. The exclusion of the ulcer from the remainder of the upper gastrointestinal tract has been advocated as a safer procedure for certain patients. One of the great advantages of resection with exclusion of the ulcer is the elimination of the passage of the gastric juices over the ulcer bed. This is an important factor in the prevention of digestion of blood clot, resulting in recurrent hemorrhage.

The purpose of this paper is to demonstrate further that in the occasional case of massive bleeding from a peptic ulcer, a conservative surgical plan can be utilized to advantage and with a successful outcome. We wish to emphasize further that we still subscribe to subtotal gastrectomy with removal of the bleeding ulcer if at all possible and provided that the condition of the patient at operation is favorable for this procedure. A conservative plan has been used in the following two cases and we wish to present these cases in detail since they present two different types of situation. In one instance, conservative surgery is a definite procedure of choice whereas in the other it is to be avoided if at all possible.

Case 1:—Mr. G. C., a 60-year old sportswriter was admitted to the St. Elizabeth's Hospital, Brighton, Mass., on December 1, 1952. He had enjoyed reasonably good health except for infrequent episodes of weakness and transient fainting spells for the last 15 years. In April, 1952, he had an episode of gastrointestinal bleeding, treated by bed-rest and whole blood transfusions. In June, 1952, he again had gastrointestinal bleeding, resulting in marked anemia. Following the latter episode, a duodenal ulcer was demonstrated by x-ray. Electrocardiogram studies revealed myocardial damage. Renal function studies showed albuminuria and casts in the urine. Approximately ten days prior to admission, it was noted that he had developed jaundice with clay-colored stools, orange tinted urine, hyporexia and indigestion. Progressive weakness continued but it was reported via phone to his family physician that the jaundice was decreasing five days after the onset. He was suddenly awakened at 3 A.M. on the day of admission with the urge to defecate and passed a foul black stool. He felt very weak and recalled passing some blood by mouth. He was sent to the hospital almost immediately.

The physical examination showed a 60-year old, markedly icteric white male in a state of shock and collapse. The blood pressure was 60/46 and the pulse was 68 per minute and regular. There was a four plus icterus of the sclerae and the sublingual bed. There were no telangiectasia, purpura or

ecchymoses. The abdomen was flat. No vascular pattern was noted on the abdomen. The kidneys and spleen were not palpable. There were no other palpable abnormal masses. The liver was palpable two fingers below the right costal margin but it was non-tender. The peristalsis was active and low pitched. There was no costovertebral angle tenderness or hernia. Rectal examination showed black tarry stool on the examining finger. The extremities showed no clubbing, purpura or edema. There was a normal sensory status relative to position, vibration, pain, temperature, and pin-prick.

In spite of the administration of plasma and multiple blood transfusions, the patient continued to hemorrhage and the blood pressure could not be stabilized. Because of the uncontrolled bleeding, it was agreed that operation should be done in an effort to stop the hemorrhage. He was taken at once to the operating room where under endotracheal anesthesia, the patient was prepared and draped. A transverse incision was made in the upper abdomen,

Fig. 1—Scarred first part of duodenum.

dividing both rectus muscles transversely. No free fluid was found on opening the peritoneal cavity. The liver felt nodular; the gallbladder felt thickened and contained a single calculus measuring approximately 2 cm. in diameter. The intestines were bluish in color because of the large amount of blood within the lumen. In the first part of the duodenum there was noted a scar on the anterior surface (Fig. 1).

It was felt that the patient's condition was too poor to warrant subtotal gastrectomy. Therefore, the duodenum was opened on the anterior surface longitudinally (Fig. 2). On the posterior wall (Fig. 3), an ulcer was seen, and it appeared as if there was a small area in the central portion from which active bleeding had recently occurred.

A similar area just below the main ulcer was also seen. Both of these areas were transfixed or ligated by mattress silk sutures around the central portion of the ulcer in an effort to ligate the bleeding vessel. A piece of oxycel was placed over this area. A large amount of coffee-ground material was suctioned from the stomach. The opening in the duodenum was then sutured transversely. A piece of omentum was "tacked over" the suture line. During the operation, the patient received three additional pints of blood. At the end of the operation his condition was improved. The blood pressure was 120/80, and the skin was dry and warm.

The patient did well postoperatively, and there was no evidence of further bleeding during the remainder of his hospital stay. He was discharged on December 19th, and the treatment for his hepatitis was continued at home.

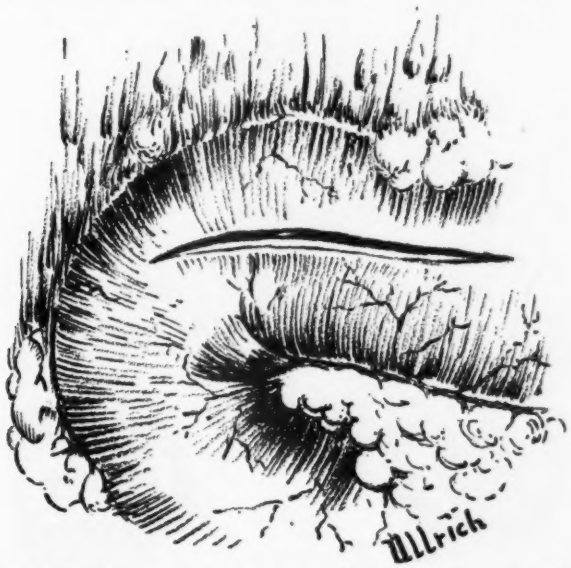

Fig. 2—Longitudinal opening on anterior surface of the first part of duodenum.

He was readmitted on December 24th, 1952, only 15 days after his first admission, with recurrent upper gastrointestinal bleeding. The pulse was 124 per minute and regular. The blood pressure was 176/110. The abdomen was soft. The liver was two finger-breadths below the right costal margin. The spleen and kidneys were not palpable. No other abdominal masses were palpable. There was an upper well-healed recent transverse abdominal incision. The hemoglobin was 5.6 gm. per cent with a hematocrit of 27 per cent. Five hundred c.c. of whole blood were administered, and the patient was placed on a one-hour chart, and blood was ordered to be replaced as needed. The blood pressure became stabilized after patient received 500 c.c. of blood. A Sippy dietary regimen was initiated and Banthine, 50 mg. given every six hours. On January 1st, 1953, he was started on Cream of Wheat, two or three times daily, and also egg

white, twice a day and these foods were well tolerated. The patient was evaluated for definitive subtotal gastrectomy, but he was discharged on Janury 7, 1953, in hope that he could further improve physically before coming back for a subtotal gastrectomy. It was also felt that the hepatitis made him a poor risk for subtotal gastrectomy. Since the latter episode of bleeding appeared to have been of moderate degree, compared to his previous admission, and as it had completely subsided at this time, nonsurgical treatment was advised for the present time.

Case 2:—Miss H. M., a 65-year old white female, was admitted to the hospital on February 15, 1953, with a chief complaint of massive hematemesis.

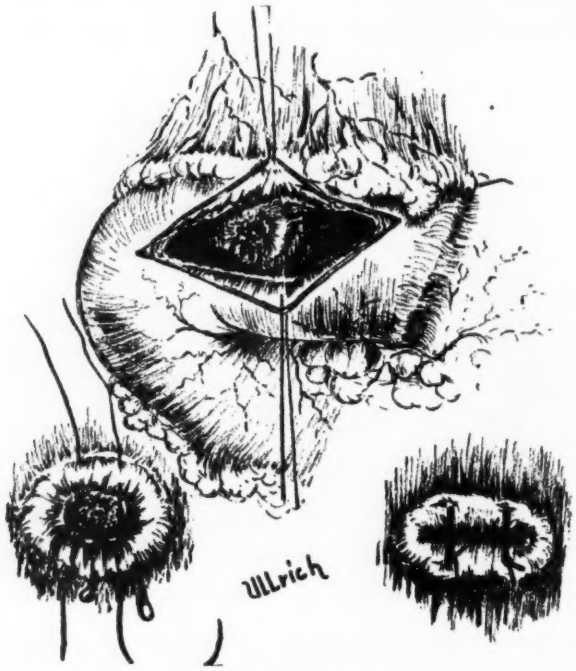

Fig. 3—With the duodenum opened, a bleeding ulcer is shown on the posterior wall. Inserts are used to demonstrate closure with black silk sutures.

Three years prior to admission, this patient was investigated by x-ray for a complaint of epigastric pain. The gastrointestinal series at that time was negative, and the patient was symptom-free until one week prior to admission at which time she noted a recurrence of abdominal epigastric pain. The pain was relieved by the ingestion of milk and other foods, but it was severe enough to awaken her at night.

On the night prior to admission the patient vomited a large amount of bright red blood and passed a large, tarry, black stool. She had never noticed black stools before. Several months ago, she coughed up some blood-flecked sputum.

Physical examination showed a very pale, elderly appearing woman, apparently chronically ill. The pulse was 100 per minute and regular. The abdomen was soft with no epigastric tenderness. A rectal examination demonstrated black, tarry stool on the examining finger. She was given several blood transfusions but because the bleeding did not appear to be controlled, it was deemed advisable to subject the patient to operation. On February 18th, 1953 she was taken to the operating room in very poor physical condition. She had been bleeding very profusely and her general condition gradually became worse. A right rectus incision was made, and exploration of the stomach showed a large ulcer situated high on the lesser curvature (Fig. 4).

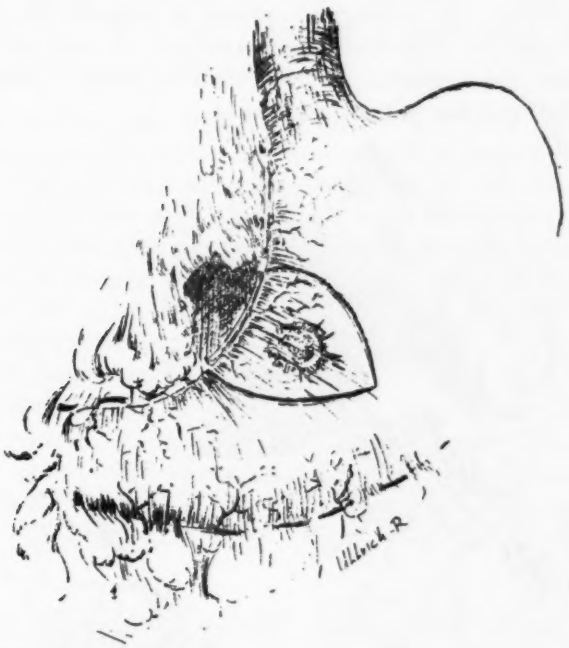

Fig. 4—Artist's conception of ulcer on lesser curvature of stomach and area that should be removed.

Close to the diaphragm the remainder of the stomach appeared quite normal with no evidence of malignancy. The duodenum appeared free of ulceration. The small bowel appeared bluish-black in color because of the free blood in its lumen. A V-shaped portion of the stomach was excised at its upper end which included the ulcer (Fig. 5).

The wound was closed and the patient returned to the ward in good condition. The patient was given blood throughout the operation, and her condition was felt to be about the same as when she entered the operating room. The pathological report showed that the patient had a benign gastric ulcer with arteriosclerotic vessels "feeding it". She made an excellent postoperative recovery,

and there was no further evidence of bleeding. She was discharged on March 3rd, 1953, much improved.

Conclusions

In Case 1 a subtotal gastrectomy was carried out to cure permanently the patient of his bleeding ulcer. The element, however, is an elective one, that is to say when the general condition of the patient warrants prolonged surgery. Furthermore, it would have been extremely risky to have subjected this patient to a subtotal gastrectomy because of his poor general condition secondary to massive hemorrhage which was complicated by hepatitis. In spite of the fact that this patient, Mr. G. C., had a recurrent episode of hemorrhage, presumably from the same site following a conservative procedure, it was successfully treated by medical means and definitive surgery could be further postponed until that time when one felt that the patient was ready.

Figs. 5 and 6—Demonstrate area resected (including ulcer) and manner of repair.

In Case 2 the immediate source of bleeding was eliminated by a "V-section" of that portion of the stomach bearing the ulcer. The patient's (Miss H. M.) general condition was too precarious to do otherwise. Again it was felt that after improvement of the patient's general condition and following complete recovery from the effects of so-called "chronic shock" due to prolonged severe hemorrhage, subtotal gastrectomy may be more wisely employed as the definitive secondary procedure.

A perusal of the literature shows that conservative surgery for massive gastroduodenal hemorrhage is not a new concept. Until ten years ago, it was frequently used as a means of controlling severe gastric and duodenal ulcer hemorrhage. There is no question but that today in the greater majority of the cases, a subtotal gastrectomy can and should be performed. Subtotal gastrectomy is certainly the better of the two procedures provided that the general condition of the patient at the time of operation warrants it. When it is sensed that the condition of the patient is one where subtotal gastrectomy would be unusually hazardous, then it is justifiable to resort to a less formidable procedure although admittedly less curative. In a way, we can compare this less formidable procedure to the need of the occasional cholecystostomy in acute cholecystitis in preference to cholecystectomy when the risk of a definitive procedure is too deleterious for the patient's welfare.

Amongst the various conservative procedures that have been advocated for massive bleeding ulcer, Arthur Allen of Boston had advocated the ligation of the pancreaticoduodenal artery along with duodenotomy and the direct plication of the ulcer. This procedure is still of value as a last resort. Warren Cole believes that if the patient is elderly and his physical condition precarious, it is preferable to control the bleeding locally by various methods and contemplate a subtotal gastrectomy at a later date. He recommends that the ulcer be visualized by a generous pylorotomy and duodenotomy. If the ulcer is on the posterior wall, penetrating into the pancreas, then the bleeding usually comes from the pancreaticoduodenal artery. He states that the conservative procedure should include the ligation of the gastroduodenal artery in normal tissue. The vessel must be ligated above and below the ulcer. He also emphasizes, however, that the ulcer bed should also be plicated by transfixion silk sutures. Silk sutures are preferable to catgut inasmuch as gastric juices are more apt to digest catgut more rapidly than silk.

Finsterer and Heuer first advocated excision when one encounters a bleeding gastric ulcer. Ligation of the right and left gastric arteries in conjunction with a wedge excision of the ulcer will be sufficient to curtail bleeding in the extremely poor risk patient. These authors emphasize that a subtotal gastrectomy at a later date will be indicated because of the strong possibility of another gastric ulcer forming at a later date. In massive hemorrhage from a duodenal ulcer eroding into the pancreas, Finsterer has described a method of tamponage directed towards the bleeding ulceration in the pancreas. After the bleeding is controlled by the latter procedure, he performs a secondary gastric resection.

Gray and Sharpe recently have stated that there is still a place for the Devine exclusion operation in instances of massive hemorrhage in which the complete operation of subtotal gastrectomy cannot be done. The stomach is simply transected at the angle, the pyloric segment closed and a retrocolic, complete, terminolateral gastrojejunostomy is performed. The consensus of many surgeons,

however, seems to be against the performance of the Devine exclusion operation in any situation occurring in the stomach.

The postoperative care of the patient following the conservative surgical treatment for massive gastroduodenal hemorrhage entails the use of gastric decompression by Wangensteen suction for about 24 to 48 or 72 hours. This regimen is followed by a progressive postoperative ulcer diet. If bleeding subsides completely without surgery, one must inform the patient that as soon as his general condition warrants, a subtotal gastrectomy should be performed at a later date.

Summary

1. Two cases of massive hemorrhage from peptic ulcer are described in detail. Because of the poor general condition of the patients, conservative surgical therapy was carried out in order to control the bleeding site.

2. Subtotal gastrectomy with removal of the distal two-thirds of the stomach including the pylorus is the ideal procedure for massive upper gastrointestinal hemorrhage. It is still recommended as a definitive procedure following conservative therapy as soon as the general condition of the patient warrants further operative intervention.

3. Conservative surgical therapy should consist of complete excision of the ulcer in the case of a bleeding gastric type. The ideal conservative management of massive bleeding from a duodenal ulcer is as yet unknown. If the condition of the patient warrants it, subtotal gastrectomy should be carried out. Plication of ulcer beds and ligation of adjacent blood vessels are at best poor procedures and are to be avoided if at all possible.

We wish to express our appreciation to Dr. John Spellman for allowing us to use one of the case reports.

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THE DRUG OF CHOICE IN AMEBIASIS*

KERMIT G. DWORK, M.D.†

Forest Hills, N. Y.

For the last 20 years amebiasis has been the infection which has evoked the greatest interest from American parasitologists because of its incidence, problems of diagnosis, and advances in treatment.

The discovery of *Endameba histolytica* by Loesch in 1875 occurred, appropriately, in a city far removed from the tropics, but for the next 60 years amebiasis was thought, curiously enough, to be restricted to the hot counrties of the world. The name of the city of discovery, St. Petersburg, has since been changed to Leningrad. The name of the parasite, *Ameba coli,* has since been changed to *Endameba histolytica* and the treatment has changed from ipecac (which it will be recalled, contains about 2 per cent of emetine) to a solid array of at least 10 drugs of imposing effectiveness.

The medical dictum that when a number of different treatments is in current use for any disease none of them is effective, is belied by the 80 to 90 per cent rates of cure which seem to follow the use of modern amebicides.

Before proceeding further let us determine what is meant by the term "rate of cure" as applied to amebiasis. Observation over many years has demonstrated repeatedly that during treatment most patients are relieved of symptoms and that examination of the stools immediately following treatment fails to reveal the presence of amebae. As time goes on a few of these patients complain again of the same symptoms, and the stool again contains the parasite. The recurrence of symptoms and findings becomes manifest in even more patients later. This fact—the increasing increment of recurrences with time—should justifiably color our concept of the "rate of cure". That is why conclusions as to the value of a new drug should be primarily based on the results of long term follow-up. Further, that is why re-examination should be conducted at intervals following treatment for, let us say, one year.

Now we come to that treacherous term of tropical medicine: "The Drug of Choice".

The individuals drugs that are in widest use today are the following:

1. Antibiotics: Aureomycin, Terramycin, and fumagillin.
2. Iodohydroxyquinolines: Diodoquin, Vioform, and Chiniofon.
3. Arsenical: Carbarsone.
4. Bismuth-arsenic: Milibis.

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†Instructor in Tropical Medicine, School of Public Health, Columbia University.

5. 4-aminoquinoline: chloroquin.

6. Alkaloid: emetine.

To begin with let us consider the antibiotics. In 1949 when McVay and his colleagues discovered the usefulness of Aureomycin in this disease[1], satisfactory but not total rates of cure had already been obtained with Carbarsone, Diodoquin, Vioform, and Chiniofon. Since that time we have been besieged with a succession of mold products, the effectiveness of which cannot be denied, but the limitations of which are equally apparent to the critical observer.

For example, most physicians who have prescribed Aureomycin or Terramycin for numerous patients have observed abdominal pain, nausea, vomiting, diarrhea, and anal pruritus result from its use. These undesirable side-effects are sometimes severe and surprisingly persistent following discontinuance of the drug. I have gotten the strong impression that when amebic colitis is treated with Aureomycin in standard dosage the incidence of these troublesome side-effects is higher than when this drug is used in other conditions. The treated patient may be grateful that a new antibiotic has poisoned his amebae, but often enough he was less troubled by the parasite than by the diarrhea, pain, and perineal irritation caused by the drug.

It is a fact that Aureomycin, Terramycin, and fumagillin are among the best of amebicides. Yet the initial enthusiasm following the results of short term study of these drugs was somewhat tempered as recurrences were detected among the patients followed for four or more months. Significant evidence of the increasing number of recurrences with long-term follow-up is recorded by Shookhoff and Sterman[2] and Most and Van Assendelft[3], among others. Such is indeed the story not only with the antibiotics, but also with every one of the available drugs for treating amebiasis, and a relapse rate of 10 or 20 per cent is usually found when cases are followed adequately. Reinfection may explain an occasional instance of apparent failure of treatment, but for most relapsing and refractory cases the explanation can at present be only conjectural.

The latest antiamebic product of the mold is fumagillin, and the impression has been gained from some sources that here, at last, is the end of the road for amebae—here, at last, is "The Drug of Choice". This, I am sorry to say, does not appear to me to be the case. It is certainly true that this drug is amebicidal *in vitro* in extremely high dilution. *In vitro* activity of amebicides, however, is very frequently at variance with clinical results, and the response of the patient is the only reliable evidence of the clinical value of a drug. Another stated virtue of fumagillin is its apparent specificity as an amebicide and not as a bactericide. Let us examine this a bit closer by considering the important role of bacteria in amebic infections.

Endameba histolytica is a protozoan which owes its survival in part to the availability of mechanisms—perhaps enzyme systems—outside of itself. We see

this amply demonstrated in the fact that they will not survive and reproduce in the test tube unless the culture is contaminated with viable bacteria—or, as Phillips[4] has shown—with *Trypanosoma cruzi.* Death of these contaminants invariably means death of the amebae. The fact that amebae can survive in the liver of the human host where the environment may be completely free from bacteria may mean only that *this* environment provides a factor—perhaps enzyme mechanism, perhaps chemical—which is otherwise supplied by bacteria. Numerous experimental studies from 1891 until the present have incriminated bacteria as a most important accessory to the invasiveness and pathogenicity of amebae. In clinical practice this dependence of the ameba on bacteria for survival has been strongly suggested time and again by the marked but temporary improvement seen in patients with amebiasis of the colon following the use of such antibacterial agents as penicillin, sulfonamides, and streptomycin. Many parasitologists are therefore of the opinion that bacterial invasion of the amebic ulcer of the colon is a constant and important factor in the pathogenicity of this protozoan. In the light of these observations, such drugs as Aureomycin and Terramycin may provide a double attack on the amebae and bacteria simultaneously. By the same token the apparent lack of bactericidal activity of fumagillin is a somewhat dubious virtue. Nevertheless fumagillin is undoubtedly a potent amebicide.

Let us now examine the results of clinical use of fumagillin. McHardy, Bechtold, and Welch[5] treated 64 cases and with a 4 to 8 month follow-up period reported 3 recurrences, a cure rate of 95 per cent. They used a dose of 60 mg. daily, which is higher than that usually recommended. Anderson and co-workers[6] cured 13 out of 20 patients—a cure rate of only 65 per cent, but they used small doses of the drug. Between these two extremes, a number of studies revealed a rate of cure that averages perhaps 90 per cent.

Our own experience with fumagillin at the Tropical Disease Diagnostic Service may be summarized as follows: In our initial trials because of unfamiliarity with the drug and fear of toxicity we used what we now know to be inadequate doses. In the last 12 cases that we treated with fumagillin, however, doses were with one exception, 10 mg. three times daily for 10 days. Follow-up in 10 of these cases 2 to 4 weeks later showed negative stools in 9 of the 10, but one was persistently positive. Repeated follow-up of these patients after 6 months may well reveal the reappearance of E. histolytica in a few other cases. Side-effects such as palpitation, dizziness, drowsiness, and epigastric distress were encountered but they were not severe and did not force discontinuance of the drug. In our limited study fumagillin therefore appears to be a potent amebicide the use of which may be attended with undesirable but not serious side-effects, and which results in a high but not total rate of cure.

As to other antibiotics—Aureomycin and Terramycin are effective amebicides, Terramycin perhaps being somewhat superior. They do not, however, exert their highest efficiency unless given in top doses, which usually means 2 gm.

daily for 7 days. At this level toxic side-effects are frequent and often severe. As a rule this large dose cannot be continued for more than a few days. In the case of Aureomycin when the dose was lowered to 1 gm. daily for 7 days, our failure rate rose to 16 per cent in a group of 42 cases. Numerous studies of Aureomycin and Terramycin in other hands have shown a rate of cure of between 80 and 90 per cent.

How do the iodohydroxyquinolines compare with the antibiotics? Out of 152 adult patients whom we treated with Diodoquin, 16 (11 per cent) showed positive stools at some time after treatment. Six of these 16 cases, however, had inadequate doses of the drug. The cure rate with Diodoquin was therefore over 90 per cent in adults. Similar results were obtained with 57 children.

As to Chiniofon, there were 11 failures in a group of 65 adults and children, 4 of the failures following inadequate dosage. The cure rate in this series is therefore about 85 per cent.

Our Vioform data are incomplete, but in a group of 20 cases followed for 1 month there was one failure.

It is my impression that Diodoquin is the most dependable of these quinoline compounds, and that Vioform is somewhat more effective than Chiniofon.

Antibacterial agents such as penicillin and sulfonamides also enter the picture because of their occasional usefulness in diminishing the bacterial content of the bowel, preparing the field, as it were, for the more efficient amebicides. In this connection, Armstrong, Wilmot, and Elsdon-Dew[8] found in short term studies that the best results of numerous schemes of treatment were obtained when penicillin and sulfasuxidine were given first and then followed by emetine and Diodoquin. Other combinations of drugs used simultaneously have been tried by numerous investigators, but the evaluation of their effect has been difficult.

With this as a background, then, what is "The Drug of Choice" in amebiasis? It will not come as a surprise that there is *no* drug of choice for this disease. There are, fortunately, several drugs of choice, and the choice in any given case should be dictated by such considerations as *previous failure of a given amebicide, history of sensitivity to the drug, severity of symptoms of the disease, presence of amebic hepatitis, necessity for rapidity of treatment, certainty of diagnosis, and the financial status of the patient.* For example, a food handler who is kept from work because of the discovery of amebiasis might well be given Carbarsone because of the short duration of treatment and the relative inexpensiveness of the drug. On the other hand, for the patient with severe dysenteric symptoms (fortunately, unusual in this country) where it is felt that the most energetic measures for the relief of symptoms are called for, one might start off by giving Emetine. This drug may be given in one-grain doses by injection daily for 5 to 8 days, bearing in mind always that although the effect on the patient's

symptoms are immediate and dramatic the toxicity of the drug upon the cardiovascular, nervous, and gastrointestinal systems is cumulative. Emetine is useful also in certain patients as a therapeutic test. This drug, however, has a very low rate of absolute cure, and must be followed by one of the intestinal amebicides in order to avoid the real risk of recurrence of the disease.

To come back to the question of choice of drug, one should not prescribe any of the "mycin" antibiotics for the patient who has a history of nausea, vomiting, diarrhea, abdominal pain, or anal pruritus following his previous use of that drug. For general use, Diodoquin is a good amebicide, and does not usually cause undesirable side-effects. Milibis is likewise a satisfactory general amebicide although the failure rate in children seems to be high. Treatment with Vioform results in a somewhat higher incidence of undesirable gastrointestinal symptoms. Fumagillin is a potent amebicide and its exact place in the scheme of treatment must await continued evaluation. Aureomycin and Terramycin are effective amebicides but their use is attended with a high incidence of undesirable side-effects and they are expensive. Terramycin may be the more efficient of these two.

In broad perspective, perhaps most of the cases seen in this country will best be managed with a course of Diodoquin or Carbarsone. A certain number will do well on fumagillin, Terramycin or Aureomycin. The sicker minority of patients might well be treated with penicillin or sulfasuxidine followed by Diodoquin. The seriously ill cases should be given emetine either before or concurrently with the standard amebicides.

For those 10 or 20 per cent who relapse following treatment, further medication is in order. In those cases it would seem best to choose an amebicide different in type from the original one used. In these refractory cases one may also use combinations of amebicides given concurrently.

Time, unfortunately, does not permit more than a few words to be said about the effect of chloroquin on amebic liver disease. We know that it is a reliable agent for amebic hepatitis and that it cures over 90 per cent, but not all, of these cases. Because of its uncertain effect on amebic colitis (in which condition it cures only about 50 per cent of the cases) it should not be used in amebic infections which are limited to the intestine. With its use a few patients will exhibit ocular and central nervous system side-effects, sometimes of pronounced degree. One of the standard drugs efficient against intestinal amebiasis should always be given concurrently or after completion of the course of chloroquin.

Regardless of the treatment used, the next step should be the same in every case: re-examination of the stools must be done at intervals for a period of six months to a year. In this regard it is inadvisable to do stool studies in less than two weeks after the completion of treatment inasmuch as practically every case will have negative stools immediately following the use of a potent amebicide.

The variety and effectiveness of available amebicides leave little to be desired, but the perfect drug has yet to be discovered. Such a drug should have a margin of safety and freedom from undesirable side-effects greater than most of those now available. It should eradicate the symptoms of amebiasis immediately, and be permanently curative against 100 per cent of cases, including those with extraintestinal metastatic infections. It should also be inexpensive, and require but a short time for a course of treatment.

With these desirable qualities as an unattained goal, we nevertheless today may be assured of curing 8 or 9 out of every 10 of our amebiasis cases, if not with a drug of choice, certainly with a choice of drugs.

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Discussion

Dr. Howard B. Shookhoff (New York, N. Y.):—Dr. Dwork has given you a clear statement of the complexities of choosing the proper therapy in amebiasis. Unless one is motivated by some partisan interest, it is not easy to state categorically what is the best treatment. Certainly, one cannot emphasize too much his point that the best treatment for one case is not necessarily the best for another.

One reason why it is difficult to choose the best therapy for a given case of amebiasis is that there is a paucity of really satisfactory comparative data on the results of therapy with individual drugs and especially with combinations of drugs. Frequently, a new drug is reported and compared with published results of older drugs without regard for the type of case treated. The results of any therapy in severe ulcerative dysentery will necessarily not be as good as in cases with mild symptoms and negative sigmoidoscopic findings.

Another criticism of many published reports is that reliance is placed on the examination of casual rather than fresh, warm stools. Positive findings are far more frequent where fresh diarrheal stools are examined.

Dr. Dwork has already referred to the importance of an adequate period of follow-up. I realize that it is difficult to get patients to come back repeatedly over the period of six months to a year, yet the attempt must be made if we are to acquire satisfactory data.

As new reports appear in the literature, I urge you to scrutinize them carefully before accepting the conclusions put forth.

In any discussion of the treatment of amebiasis, it seems fair to point out that you must catch your ameba before you can kill it. It is rarely justifiable to treat patients for intestinal amebiasis unless the organism has been demonstrated in the stools. The clinician need not be expert in the morphology of the amebae, but he must see to it that the laboratory technician has the best opportunity to exercise his special talents in finding the organism if it is present. This means not only persuading the patient of the importance of warm stool examinations, but also refraining from administering medication which will interfere with getting the best out of the laboratory.

In this connection, I call your attention to Dr. Dwork's remarks concerning the antibiotics, especially Terramycin and Aureomycin. Whether or not you favor using them in treatment of amebiasis, you must recognize that they can suppress or cure amebic colitis. In small doses they are more apt to inhibit the multiplication of the amebae without curing the infection. This suppressive action may persist for some time. Hence, the practice of treating diarrhea with a little Terramycin or Aureomycin is to be decried. Even the administration of sulfonamides may depress the amebae below the point at which the laboratory can detect their presence. The action of sulfonamides, however, is much more transient than that of the antibiotics.

Dr. Max M. Sterman (New York, N. Y.):—Dr. Dwork has very ably and succinctly presented to you the overall picture of the management of intestinal amebiasis. In my opinion, the choice of the initial amebicide is not the most difficult task. In the average case of amebiasis, as we see it in this part of the world, it really does not matter very much which one of the standard amebicides one chooses to administer. In the great majority of cases we find that one course of any of the standard drugs is ample to effect a clinical as well as a bacteriological cure. In some cases a second course is indicated, and in these cases it is preferable to change the type of drug to avoid any possible cumulative toxic effects.

There are, however, a small percentage of cases that tax our medical skill and ingenuity to the utmost. We see a number of cases who improve after a standard course of treatment, but who return to us several weeks or months later with a woeful tale of complete recurrence of symptoms, and not too infrequently an additional disturbing pruritus ani. In the majority of this group a recheck of warm, purged stools yields negative results. Yet, to all intents and purposes these patients present the clinical picture of recurrent intestinal amebiasis. These are usually clinical relapses. Assuming that all efforts are made,

as far as is humanly possible, to rule out the presence of amebic hepatitis or some other associated organic condition, we are then confronted with the problem of whether we are dealing with a straight-forward clinical relapse, or whether some other mechanism is causing these symptoms. It is in this group of cases that most of the difficulties are encountered, and in which judicious management is of the utmost importance.

Treatment must be individualized after careful evaluation of signs and symptoms. Very frequently, nonspecific supportive measures are indicated in addition to specific therapy.

Dr. Dwork has wisely omitted from his discussion the thioarsenites. In my opinion, these drugs are much too toxic and have no particular advantage over the long array of drugs at our disposal.

Perhaps the use of bacitracin should be mentioned. In our experience, we have found it to be reasonably effective and much less prone to produce side-effects which are disturbing to the patient. More work should be done with this antibiotic, especially in combination with other chemotherapeutic agents.

President's Message

The reception accorded the announcement of the founding of the American College of Gastroenterology has been most gratifying. The organizations which have been invited to designate representatives for election to our Board of Governors are presenting the invitations to their respective governing boards.

Our new Board of Governors is in the process of formation and the nominees are being selected.

A meeting of the Board of Trustees of the College was held in Washington, D. C. and the final program for the Convention and Postgraduate Course have been approved.

All indications would seem to suggest that our Convention will be the best we have ever had. The spirit of cooperation and unity prevailing is most gratifying.

However, gratifying these factors may be, the crucial test lies before us. How will our Fellowship accept the new organization and how much effort and sacrifice of time will they extend to assure the success of the College? These are questions which are all important.

I hope, therefore, when the Fellows, Associate Fellows and Members are called upon to contribute their share of cooperation, they will respond in the same way that your officers and trustees have done.

What do we expect from our membership?

First, we seek your loyal cooperation and help in familiarizing yourselves with the new aspects of the College. Read the Constitution and By-laws and see for yourselves the new and higher standards set for membership and advancement.

Second, be sure to participate in the promotion of the College by appointing yourself a committee of one to do your share.

Third, if you have suggestions for improvement, please present them for consideration.

Fourth, come to the Convention and participate in the work of the College.

Sigurd W. Johnson

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1. ROGERS, M.P., AND GRAY, G.L.: AM. J. DIGEST. DIS. 19:180 (JUNE) 1952.

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1. Reich, C., and Mulinos, M. G., Treatment of Refractory Nutritional Anemias with Gelatine. Bull. N.Y. Med. Coll., March, 1953

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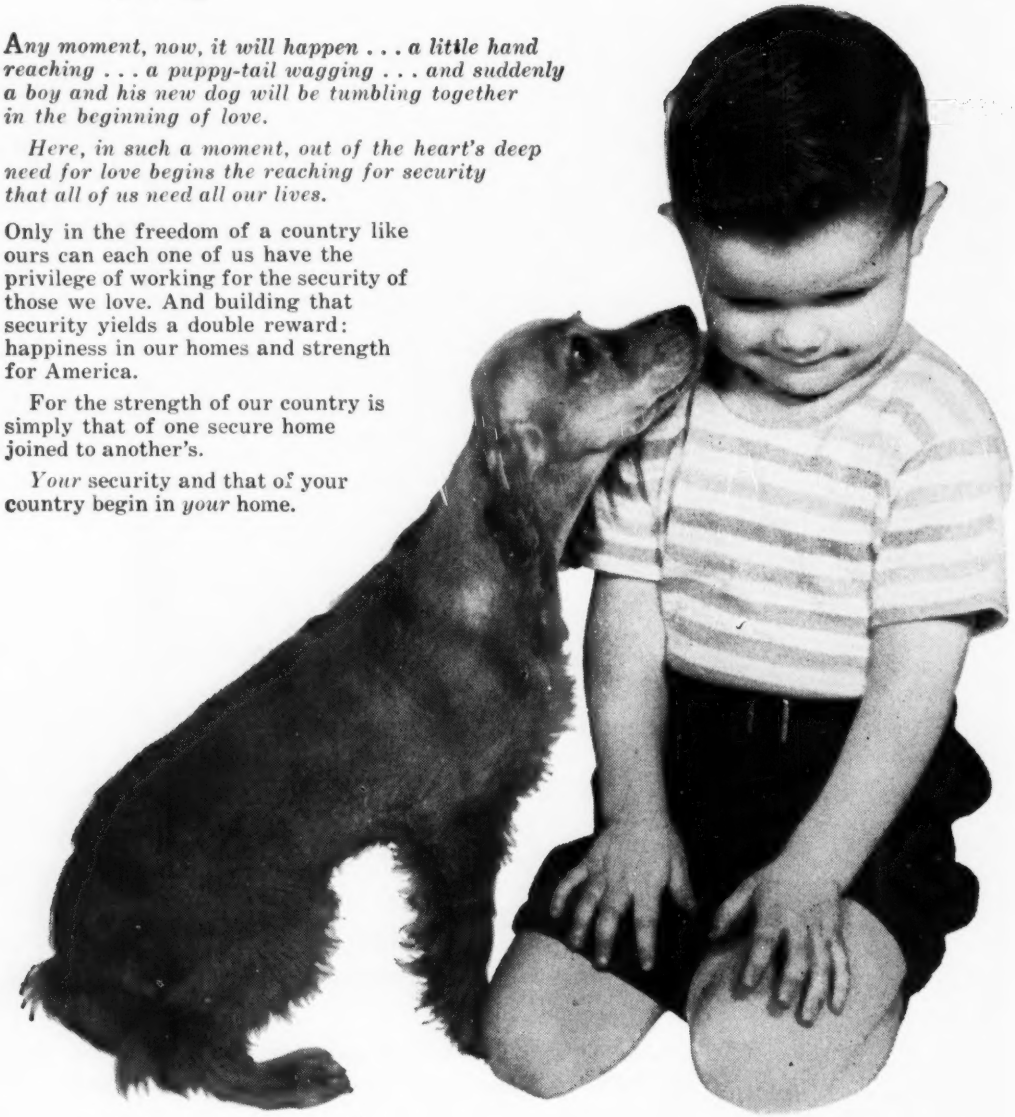

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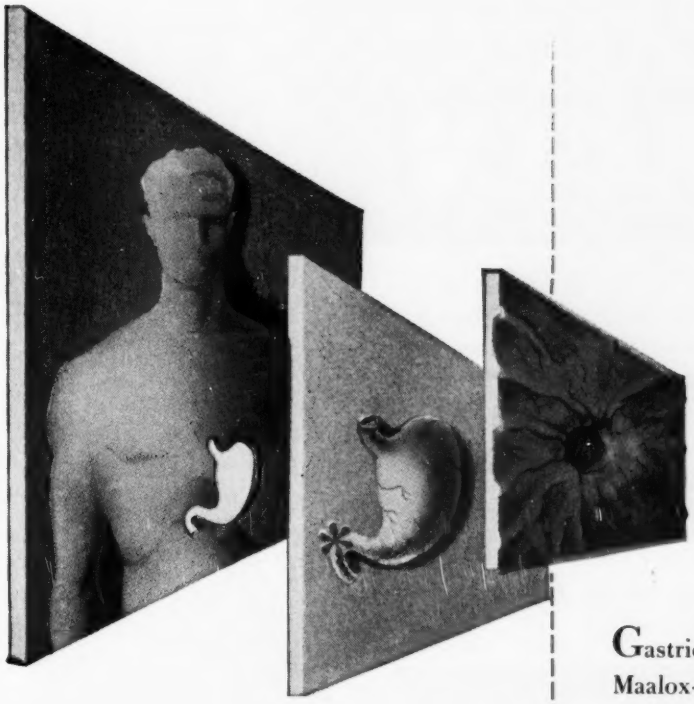

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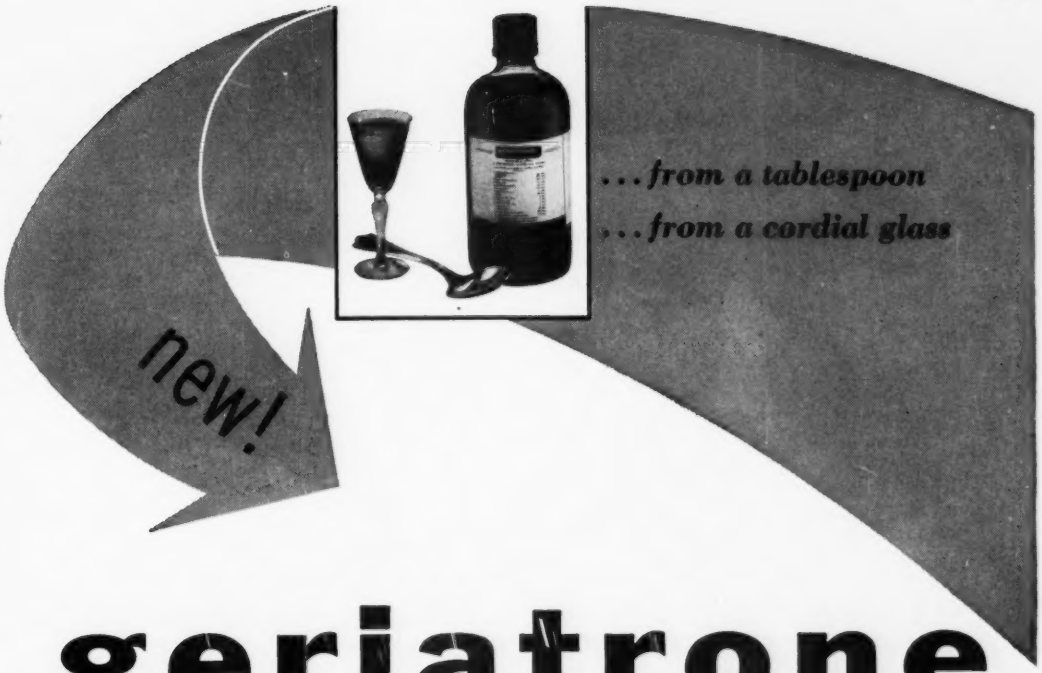

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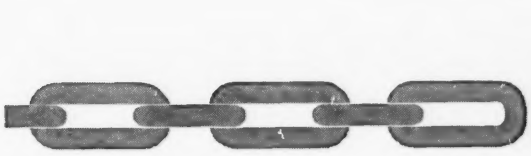
*Sherber, D. A.: The Control of Bleeding. Am. J. Surg. *86*:331 (Sept.) 1953.



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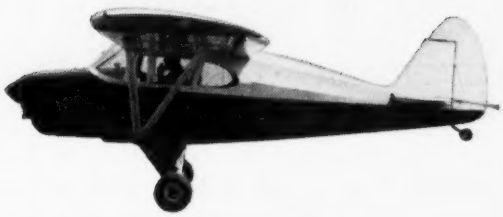

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1. Rossett, N. E., and others: Ann. Int. Med. 36:98 (Jan.) *1952*

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